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14. ABSTRACT
The general objective of the Ohio Army National Guard Mental Health Initiative is to evaluate the relationships between resilience and risk factors, both cross-sectionally and longitudinally, before, during, and after deployment in the Ohio Army National Guard. The primary project collects long-term data on a random representative sample of N=3457 service members per year in the OANG, both treatment seeking and non-treatment seeking. Since 2006, the primary objective of the OHARNG MHI was designed to function as the template upon which other projects, including but not limited to those of a translational research nature, will be superimposed. Over the past year, six manuscripts have been published, with 5 others currently under peer review. The OHARNG MHI has an established track record and solid infrastructure in place to address substantive questions in both basic and applied science. Most importantly, this project has provided the military with novel, long-term, prospective data on the National Guard, traditionally an understudied military population. This project has in the past and will continue in the future to provide the TAG, aTAG, and commanders of the Ohio Guard with useful, pragmatic information immediately relevant to the training of men and women in the Ohio Reserve Component.

15. SUBJECT TERMS
Risk, Resilience, Combat, Posttraumatic Stress Disorder, Ohio National Guard, Mental Health, Genetics, Alcohol Use Disorders, Suicide

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Ohio Army National Guard Mental Health Initiative: Risk and Resilience Factors for Combat-Related Posttraumatic Psychopathology and Post Combat Adjustment

Annual Report, September 2013

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<p style="text-align:center">Annual Report, September 27, 2013</p>

INTRODUCTION

Previously conducted research has demonstrated that deployment accompanied by combat experience results in increased risk of posttraumatic psychopathology and other mental health conditions. The general objective of the Ohio Army National Guard Mental Health Initiative is to create a research infrastructure capable of supporting a series of projects that evaluate the relationships between resilience and risk factors, both cross-sectionally and longitudinally, before, during, and after deployment. The primary project will collect long-term data on a random representative sample of at least 3,000 service members of the Ohio Army National Guard, both treatment seeking and non-treatment seeking. Research visits will be conducted at study entry and every 12 months, interviews began in November 2008 and will continue through 2018 if additional funding is secured. The Telephone Survey will be completed on all main project participants, and 500 of these participants heretofore also had an in-depth In-Person Interview once annually during waves once through 4, but this component of the study will be discontinued on the prior guidance provided by of COL Castro. The Genetics Repository collects a DNA saliva sample from consented participants in the main project. DNA samples were collected from May 2010 to January 2013 and will resume if additional funding is secured.

BODY

The OHARNG MHI is designed to study the relationships between 1) pre-existing mental illness/substance use disorders, 2) deployment to Operation Iraqi Freedom (OIF) or Operation Enduring Freedom (OEF), and 3) post-deployment related mental health and overall psychosocial adjustment and functioning. The study evaluated several groups of the Ohio Army National Guard: those deployed to OIF (Iraq, Kuwait, or Qatar), those deployed OEF (Afghanistan), those deployed to other theaters (Bosnia, Turkey, Uzbekistan, Kosovo, on a ship, or other), those deployed domestically, and those not deployed.

The OHARNG MHI has demonstrated rapid scientific progress, successfully collecting 4 waves of longitudinal data. This project conducted annual assessments on 3,457 members of the Ohio National Guard between 2009 and 2012 and in-person survey assessment on 672 of these Ohio National Guard members (as of January 31, 2013 the in-person survey component was terminated). With additional funding to complete Waves 5-9, the primary platform (telephone survey) will provide an unparalleled longitudinal sample of National Army Guard soldiers. In addition, the primary platform will be able to continue

supporting the ancillary translational research projects that fall under the auspices of the OHARNG MHI, including 1) Genetics Repository (Liberzon) 2) fMRI (Liberzon and Tamburrino) 3) Intelligent Automation Inc. (Wang) and 4) recently MOMRP-funded project 13277015 entitled: Early Intervention to Reduce Alcohol Misuse and Abuse in the Ohio Army National Guard (Blow and Calabrese).

OHARNG MHI Sites
The team of individuals and infrastructures committed to this project is extensive and prioritize a meaningful reporting relationship to the leadership of the Ohio National Guard, The Ohio Adjutant General Deborah Ashenhurst and Assistant Adjutant General of the Army BG John Harris, through the Guard's OHIOCARES Workgroup and addition in-person meetings. The Coordinating Center Principal Investigator (PI) of the Ohio Army National Guard Mental Health Initiative is Joseph R. Calabrese, M.D. and the Scientific Principal Investigator is Sandro Galea, M.D, DrPH. The Initiative includes a Coordinating Center based out of University Hospitals Case Medical Center (UHCMC) affiliated with Case Western Reserve School of Medicine (Dr. Calabrese), and six operating research sites including University Hospitals Case Medical Center, Columbia University Department of Epidemiology (Dr. Galea), the University of Toledo (Dr. Tamburrino), a research survey firm 25 years of experience with the military, Abt SRBI, Inc., the Ann Arbor VAMC Department of Psychiatry at the University of Michigan (Dr Liberzon).

Michigan State University's Biomedical Research and Informatics Center - BRIC (Dr Reed) has been involved with the project beginning in 2008 through January 2013, Prior January 31, 2013, the BRIC provided support for all aspects of informatics relevant to the In-Person Survey component of the study, including assessments, data entry and management privileges, enrollment privileges, survey building privileges, etc. Since January 2013, the role of the BRIC predominately focused on data cleaning and compiling the in-person data sets for analyses and manuscript preparation. As of August 5, 2013, David Fink, a full time data analyst, was hired at Columbia University to serve as an analyst for this specific component of the study.

Dr. Calabrese is the coordinating principal investigator of this project and the UHCMC Coordinating Center is responsible for all aspects of project coordination (scientific, administrative, and fiscal), as well as the project's interface with the leadership of the Ohio National Guard (ONG). With Dr. Galea as Scientific PI, Columbia University Department of Epidemiology responsibilities include, but are not be limited to, the design of the project's field procedures, including the annual Telephone Survey, scientific manuscript preparation, DoD and NIMH grant applications, etc. Dr. Galea also serves as the primary interface between the project and the survey firm, Abt SRBI, which carries out the telephone surveys. The University of Toledo provides leadership, has conducted in-person assessments of 200 service members in their local communities, and has special issue in gender issues. The University of Michigan Ann Arbor VA Department of Psychiatry is responsible for the design, implementation, and oversight of translation research, including but not limited to the Genetics Repository, which includes laboratory and field procedures for biological sample collection, processing, storage, association

analyses, etc. Up until January 31, 2013, the Michigan State University Biomedical Research Informatics Center provided all aspects of informatics needs for the In-Person Survey assessments, including data entry and management privileges, enrollment privileges, survey building privileges, etc. As previously stated, MSU's role as of February 1, 2013 has been to prepare the data sets for analyses.

Project #1: Primary Platform

The primary study (Project #1) within this initiative is a clinical epidemiology and health services project and is designed to function as the template upon which other projects, including but not limited to those of a translational research nature, have been superimposed. The first three specific aims of the primary research project were designed to build support and stimulate additional interest in the study of the role of resilience and risk in combat-related posttraumatic psychopathology and other similar adjustment problems.

> ### Specific Aims of Project #1:
> 1. To study the relationship between deployment-related experiences and the development and trajectory of DSM-IV Axis I diagnoses
> 2. To document the factors across the life-course that are associated with resilience to DSM-IV Axis I diagnoses and with better post-deployment functioning
> 3. To study the relationship between National Guard-specific pre-deployment and post-deployment factors and the risk of development of DSM-IV Axis I disorders

Data collection within the primary platform was suspended in January 2013 due to lack of funding. Should additional funding be granted for the project, the primary platform will interview at least 3,000 members of the Ohio National Guard, selected at random from the entire population of the Guard. All individuals who participate are interviewed for 1 hour by telephone on an annual basis, and began in November 2008 and will continue through 2018 if additional funding is secured.

A sub-sample of at least 500 participants of the telephone survey group was also interviewed on an annual basis and in-person, which on average lasted 2-3 hours. This sub-sample allowed both for validation of key domains employed in the phone interviews and for further in-depth study of trajectory of psychopathology in this sample. Study personnel recommended that participants bring a family member, friend, or significant other for support and assistance during the interview. The in-person survey clinically validated the telephone survey by using gold-standard structured interviews (i.e. SCID, CAPS) delivered by trained clinicians (Prescott, et al. 2013). As previously stated, the in person survey is permanently discontinued. The investigative team has just completed its fourth wave of data collection on January 31, 2013 – see research accomplishments below for total number of interviews completed. The participants have variable lengths of involvement and variable combat exposures, allowing us to suitably address the specific aims.

Research Accomplishments from the Statement of Work for Project #1:
Tasks #1 - #5 from the Statement of Work delineate the critical events that must be accomplished in order for the project to be successful in terms of cost, schedule, and performance. Task #1 has been completed, Task #2 completed in January 2013 (data collection for the telephone survey will reconvene once additional funding is secured), and #3 through #5 are currently in progress.

- *Tasks #1 and #2* – Baseline enrollment and Annual participant follow-up of at least 3,000 Ohio National Guard Members in the Telephone Survey, and 500 for the validation In-Person Survey, in order to be able to test Specific Aims #1 -3 with associated hypotheses.

Telephone Survey Enrollment		
Wave	Actual Enrollment	Interviews Completd
Wave 1 2008-2009	2,616	2,616
Wave 2 2009-2010	0	1,770
Wave 3 2010-2011	578	1,973
Wave 4 2011-2012	263	1,694
Wave 5 2012-2013*	data collection suspended due to lack of funding	
Total	3,457	8,053

In-Person Survey Enrollment		
Wave	Actual Enrollment	Interviews Completed
Wave 1 2008-2009	500	500
Wave 2 2009-2010	0	418
Wave 3 2010-2011	105	461
Wave 4 2011-2012	67	503
In-person component permanently discontinued as of 1/31/2013		
Total	672	1,882

- *Task #3* – Performance of a descriptive analysis of the data collected from the primary and sub-sample group including the prevalence of current mental illness and voluntary triage to OHIOCARES. At least one peer-reviewed publication per year will be derived from the study data.

We have performed several analyses of the data collected from the baseline sample, Year 2, Year 3, and Year 4 sample of participants. As reported previously, for baseline analyses we examined the broad range of characteristics that are hypothesized to be associated with mental health conditions, as well as potential mediators of these associations. As further analyses were completed over the past year, we presented the results at scientific conferences and submitted manuscripts for peer-reviewed publication.

Please see **Table 1** attached to this report for a table of manuscripts that have been published/In Press, under review, or under preparation. Please see **Appendix A** for the full text reprints of manuscripts published since the previous annual report in October 2012, which includes the following:

1. Marshall BD, Prescott MR, Liberzon I, Tamburrino MB, Calabrese JR, Galea S. Posttraumatic stress disorder, depression, and HIV risk behavior among Ohio Army National Guard Soldiers. Journal of traumatic stress. 2013;26(1):64-70.
2. Goodwin RD, Prescott MR, Tamburrino M, Calabrese JR, Liberzon I, Galea S. Cigarette smoking and subsequent risk of suicidal ideation among National Guard Soldiers. Journal of affective disorders. 2013;145(1):111-4. PMCID: 3701306.
3. Goodwin RD, Prescott M, Tamburrino M, Calabrese JR, Liberzon I, Galea S. Smoking is a predictor of depression onset among National Guard soldiers. Psychiatry research. 2013;206(2-3):321-3. PMCID: 3701300.
4. Fine TH, Contractor AA, Tamburrino M, Elhai JD, Prescott MR, Cohen GH, et al. Validation of the telephone-administered PHQ-9 against the in-person administered SCID-I major depression module. Journal of affective disorders. 2013;150(3):1001-7.
5. Prescott M R, Tamburrino M, Calabrese J, R., Liberzon I, Slembarski R, Shirley E. Validation of lay-administered mental health assessments in a large Army National Guard Cohort. International Journal of Methods in Psychiatric Research. 2013; In Press.

Other

Please also see **Appendix B** for the Continuing Review Report with the annual update for the local IRBs, submitted in August 2013.

- *Task #4* – Annual oversight meetings for the Initiative.

Administrative Advisory Board: The *Administrative Advisory Board (AAB)*, consisting of state and local leaders, administrators, and stakeholders providing guidance on non-scientific issues, is held on an annual basis.

The 2013 AAB meeting was postponed until October 17, 2013 because at this time the investigator's hope to hear about the Joint Warfighter Research application that was submitted on July 26th to continue Wave 5 data collection. However, the Coordinating Center PI, Dr. Joseph Calabrese met with the leadership of the Guard on March 7, 2013 to provide them with a detailed update of the project which included:

1. Review of the Original Vision for the Ohio Army National Guard Mental Health Initiative (OHARNG-MHI) circa 2005
2. Review of one Possible Vision for the Next Generation of Ongoing Research Circa 2014
3. Funding and Grant Submission Update

4. Scientific Accomplishments
5. General Findings, Implications, and Conclusions

Scientific Advisory Board
The External Scientific Advisory Board, consisting of nationally and internationally renowned individuals with strong scientific backgrounds providing critical feedback on the scientific merit of the project, is held on an annual basis. As previously reported, the most recent meeting was held on April 2, 2012. Due to limited funds, the 2013 SAB meeting was cancelled and will resume once additional funding is secured.

PTSD Biomarkers IPR Meeting
On February 19-20, 2013 Dr. Joseph Calabrese opened the PTSD Biomarkers IPR meeting in Fort Detrick. This meeting consisted of presentations from MOMRP funded investigators with a focus on PTSD and was attended by the leadership of MOMRP, including Dr. COL Castro (former Director, MOMRP) and Dr. Ron Hoover (Psychological Health Deputy Portfolio Manager for PTSD). During this meeting, COL Castro directed Dr. Calabrese to consider the extension of the Ohio project to a second platform in a different state with disparate needs compared to Ohio such as a site in California, the south, and/or the east. Please see **Appendix C** containing the slides presented by Dr. Calabrese on the OHARNG MHI.

Congresswoman Kaptur
Since 2006, Drs. Calabrese and Tamburrino have met with Congresswoman Kaptur annually to provide her with a detailed update on the progress of the OHARNG MHI. The most recent meeting took place on September 4, 2013 in Cleveland, Ohio. Most recently, Congresswoman Kaptur spoke of Dr. Calabrese and the OHARNG MHI in the House of Representatives applauding his efforts on the project. Please see **Appendix D** for the Congressional Record.

- *Task # 5* – Financial Reporting is due quarterly via SF425, and has been submitted regularly and on schedule over the past year. The most recent report was submitted on July 23, 2013 for the second quarter 2013. Additionally, the most recent Quarterly Report was submitted to TATRC and USAMRAA on July 10, 2013 for the second quarter 2013.

OHARNG MHI Ancillary Projects

Translational Research Project #1 and OHARNG MHI Project #2 – Genetics Repository
The first translational research project is the Genetics Repository component (Project #2) led by Dr. Israel Liberzon and studies genetic determinants of risk and resilience to the development of PTSD and other mental illnesses. This first translational project involves the creation of a repository of saliva DNA samples, which will be used to perform genetic association studies on selected candidate alleles and potentially genome-wide analyses at multiple levels. These may include cross-sectional genetic association analyses of pre-deployment traits, longitudinal analyses to investigate genetic markers

and functional polymorphisms involved in vulnerability to deployment-related psychiatric disorders (i.e. in case-control association analyses), as well as building models incorporating measures of deployment-related and pre-deployment environmental factors for vulnerability (i.e. gene x environment interactions). This will also allow for integrated research utilizing neuroimaging, psychophysiological, and neuroendocrine measures to investigate the effects of genetic variants on cognitive, behavioral, and physiological function at baseline and after deployment stressors.

Research Accomplishments from the Statement of Work for Project #2:

Task #1 – In order to test the 2 hypotheses in the Genetics Protocol, the participants in the Telephone Survey of Project #1 are approached to participate in the Genetics Repository and are asked to submit a saliva sample via a kit mailed to them. Regulatory approval was granted 3/16/2010 by the DoD Office of Research Protections, with enrollment proceeding as of May 1, 2010 with the beginning of the project's 3rd quarter in Wave 2, Wave 3 and Wave 4. Due to limited funding, data collection was suspended in Wave 5. Once additional funding is secured, the collection of saliva samples will resume.

Genetics Study Enrollment	
Project Year	**Total Enrollment**
Wave 1 2008-2009	0
Wave 2 2009-2010	275
Wave 3 2010-2011	701
Wave 4 2011-2012	134
Wave 5 2012-2013*	data collection suspended due to lack of funding
Total	**1,110**

Task #2 – *Upon receipt of saliva samples, the lab at the Ann Arbor VA will process them appropriately to provide genomic DNA preparation of the samples.*

It is widely recognized that studies of candidate gene studies in trauma-exposed populations have not found "main effects" of gene association with PTSD. Instead, a gene x childhood adversity (G x E) interaction in the serotonin transporter (SLC6A4), FKBP5 and RGS2 genes has been reported. Since no GWAS has yet been reported on PTSD in a military sample, we systematically recruited OHARNG-MHI participants, who agreed to link their structured telephone interview data (including pre- and post-deployment information) with their DNA sample. Deployment-related and lifetime traumatic event exposures were obtained, including childhood adversity and DSM-IV criteria PTSD. Consented soldiers provided saliva specimens and additional self-report measures. Oragene saliva collection kits were sent to participants' homes and shipped back to Dr. Liberzon's laboratory by return mail. Genotyping was performed using PCR (serotonin transporter gene (SLC6A4) 5-HTTLPR, DRD4 VNTR) and a custom 4800 SNP Illumina array, which included ~120 previously identified candidate genes, including FKBP5, RGS2, and CRHR1 genes previously implicated in PTSD, as well as ancestry informative markers. Association of previously reported variants with level of

PTSD symptoms was tested in GLM modeling of main effects of gene (SNP), controlling for levels of childhood abuse and lifetime trauma load, and also included gene x child abuse and gene x trauma load interaction terms. 80% of soldiers agreed to be sent a genetic specimen collection kit yielding 1042 returned genetic specimens. Using the highest of the available PCL scores (n = 766), an association was found between child abuse ($F_{[2,754]}$ = 12.4. p <.00001) and lifetime trauma load ($F_{[3,753]}$ = 14.9. p <.00001). Four SNPs in FKBP5 (rs1360780, rs3800373, rs9296158, rs9470080) showed SNP x child abuse interactions (all p < .007), but no main effect on PCL. The triallelic 5-HTTLPR also showed gene x child abuse interaction in a recessive model (p < .005), but no main effects. RGS2, DRD4, and CRHR1 all showed no main effects and no interaction effects for association with PCL. This initial translational project generated the first genetic association with PTSD symptoms in soldiers deployed to Iraq and Afghanistan, while replicating previous findings of G x E interaction effects in FKBP5 and 5-HTTLPR in this cohort. Furthermore these are the first genetic findings involving a predominantly white male cohort of National Guard soldiers (see figure for summary findings).

Study Findings - Genotyping

- 82% consented, 1042 soldiers returned specimens (Oragene kits) to lab
- Genotyping: 5-HTTLPR w/PCR, >3200 SNPs in candidate genes w/ Illumina array.
- Initial analyses N=854, N=57 no LT trauma; N=715 European ancestry by PCA

Replications:
G x E (childhood trauma)
- No "main effects" association w/PTSD
- Gene x Childhood trauma interaction in 5-HTTLPR and FKBP5
- Serotonin Transporter promoter "triallelic" 5-HTTLPR p = .007
- FKBP5 (rs3800373) p = .017
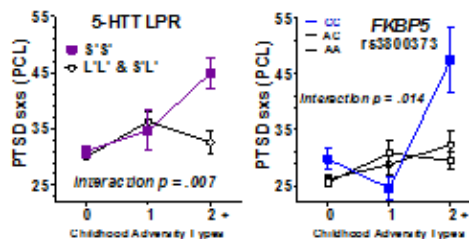
*Currently Under Review in the Archives of General Psychiatry

Much remains to be understood regarding the complex genetics of PTSD, depression, and alcohol dependence. In particular, there is need for replication and extension of prior genetic findings for PTSD and further progress in characterizing the genetic profiles of depression and alcohol dependence. Further, there are no studies to our knowledge that have investigated polygenic determinants of trajectories of posttraumatic psychopathologies and their comorbidity.

Translational Research Project #2 – fMRI Pilot Project
The **2nd translational research project** has recently begun enrollment and focuses on neuroimaging, childhood adversity, and PTSD under the leadership of Dr. Liberzon at the Ann Arbor VA and Drs. Tamburrino and Wang at the University of Toledo. To date, N=41 subjects have consented and N=19 fMRI scans have been completed on subjects from the OHARNG MHI.

Translational Research Project #3– Intelligent Automation Inc.
The **3ʳᵈ translation research project** is Dr. Roger Xu's work on diagnosis using an 'automated system'. Dr. Xu's voice-based automated Tele-PTSD Monitor system is designed to remotely screen, monitor, and provide assistance to clinicians in diagnosing PTSD. A data use agreement has been completed which allows Dr. Xu to acquire de-identified voice data obtained during the in-person validation subsample interviews conducted in Waves 1-4. These data are sent to a secure server which invokes the PTSD Scoring Engine software that statistically evaluates vocal features (e.g. pitch and jitter, etc.) to compute a PTSD mental health score. The system uses a computer-based automated scoring of voice input which makes it low cost and easily field-deployable. Recently, Dr. Xu received continuation funding from the MOMRP to continue his collaboration with Dr. Calabrese.

Translational Research Project #4– Alcohol Prevention and Intervention
The **4ᵗʰ translational research project** has recently been funded by MOMRP and is led by Fred Blow, PhD (University of Michigan and Ann Arbor VAMC). Dr. Blow has designed a randomized controlled trial of a web based easily administered intervention to advance the treatment for hazardous alcohol use which is potentially transferrable to reserve component members nationally. The application filing name is: **"OHARNG MHI: Alcohol Intervention"**, the log number is 13277015, and the unabridged title of the project is: **"Early Intervention to Reduce Alcohol Misuse and Abuse in the Ohio Army National Guard."** The project is slated to begin 1/1/2014 and enroll N=750 OHARNG MHI participants from the primary platform.

KEY RESEARCH ACCOMPLISHMENTS

1. Completion of Year 1 (beginning November 2008) of data collection
   - Telephone Survey N=2616
   - In-Person Survey N=500
2. Completion of Year 2 data collection (beginning November 2009).
   - Telephone Survey N= 1770
   - In-Person Survey N=418 interviews completed (end date December 31, 2010 per the approved protocol window)
3. Completion of Year 3 data collection (beginning November 2010):
   - Telephone Survey N=1973 interviews completed:
     - Year 3 follow up interviews: N=1395
     - Dynamic Cohort baseline interviews (closed December 2011): N=578
   - In-Person Survey N=458 interviews completed
     - Year 3 follow up interviews: N=354
     - Dynamic Cohort baseline interviews: N=104
4. Completion of Year 4 data collection (beginning August 2012):
   - Telephone Survey N=1694 interviews completed:
     - Year 4 follow up interviews: N=1431
     - Dynamic Cohort Year 4 baseline interviews: N=263
   - In-Person Survey N=503 interviews completed:
     - Year 4 follow up interviews: N=436
     - Dynamic Cohort Year 4 baseline interviews: N=67
5. Genetics Repository data collection (beginning May 2010):
   - Agreed to receive Genetics kit: N=2049 out of 2720 (75%)
   - Returned completed Genetics kit: N=1110 out of 2049 (54%)
6. 6 manuscripts have been published **over the past year**, 6 manuscripts have been submitted to peer-reviewed journals **over past year**, and 9 manuscripts are under preparation. Overall, the project has published 10 manuscripts. Please see Figure 1 for a detailed description of manuscripts published, in press, under review, and under preparation.
7. Disseminated data through 5 professional meetings (ISTSS, SBP, APA, ADAA, SER)

REPORTABLE OUTCOMES
Manuscripts, Abstracts, and Presentations

SUMMARY OF SCIENTIFIC PRODUCTIVITY

Year	Abstracts	Presentations	Published/ In Press	Under Peer Review	Under Preparation
2009	1	1	0	0	0
2010	12	14	0	0	0
2011	6	6	1	0	0
2012	7	11	3	0	0
2013	15	15	6	5	9
Total	**41**	**47**	**10**	**5**	**9**

1. Manuscripts: For manuscripts published or accepted for publication over the past year, please see Table 1. In addition, please see **Appendix A** for reprints of publications over the past year.
2. Oral presentations since the last annual report:
   a. Child Abuse and Deployment-Related Depression in the Ohio Army National Guard. Prescott M. 28th Annual International Society for Traumatic Stress Studies in November 2012.
   b. Prevalence of Sexual Trauma and Mental Health Sequelae Among Three Representative Samples. Walsh K. Annual International Society for Traumatic Stress Studies in November 2012.
   c. Alcohol Dependence and Suicidal Ideation in the Ohio National Guard. Cohen G. Psychiatric Epidemiology Training Program Seminar. December 2012
   d. Mental Health Epidemiology and the Ohio Army National Guard Mental Health Initiative. Chan P. Chronic Disease Epidemiology Lecture at Kent State University - Mental Illness in March 2013
   e. "Psychiatric Epidemiology Beyond Cells & Societies: Implications & Complications". Galea S. University Hospitals Department of Psychiatry Grand Rounds on April 5, 2013.
   f. "Military Mental Health: Focus on the Ohio Army National Guard Mental Health Initiative". Calabrese, J. PTSD 2013: In Search of a New Paradigm on April 6, 2013. – see **Appendix E** for presentation slides
   g. "Understanding the Etiology and Trajectory of PTSD across the Life Course". Galea S. PTSD 2013: In Search of a New Paradigm on April 6, 2013.
   h. "Replication of Gene x Environment Interaction in Association of PTSD with FKBP5 and 5-HTTLPR in Sample of Soldiers Deployed to Iraq and Afghanistan". King, T. Society Biological Psychiatry on May 19, 2013

i. "Neuroimaging markers in PTSD". Liberzon, I. Society Biological Psychiatry on May 18, 2013

j. "Genetic findings in ONG cohort". Liberzon, I. American Psychiatric Association 2013 meeting on May 19, 2013.

3. Poster presentations since the last annual report – see Appendix F for a reprint of the abstracts:

a. Participant Reactions to Trauma Questions in the Ohio Army National Guard (OHARNG). Fine T. 28th Annual International Society for Traumatic Stress Studies in November 2012.

b. "Molecular Genetic Approaches to Trauma Vulnerability And Resilience in Civilian and Combat Populations". King T. 2013 Anxiety and Depression Association of America (ADAA) La Jolla, CA on April 4, 2013.

c. Deployment Social Support and Alcohol Use in the Ohio Army National Guard". Chan, P. Research ShowCASE at Case Western Reserve University on April 12, 2013

d. "Association of spiritual well-being with suicidal ideation and behavior in a population-based sample of Ohio National Guard soldiers". Ganocy, S. Research ShowCASE at Case Western Reserve University on April 12, 2013

e. "Automatic Predictive System for PTSD through Hidden Associations among Survey Modules". Tashtoush, F. Research ShowCASE at Case Western Reserve University on April 12, 2013

f. "Retention Rates of a Geographically Dispersed Population Based Longitudinal Cohort of the Ohio Army National Guard". Williams, A. Research ShowCASE at Case Western Reserve University on April 12, 2013.

g. "War and civilian trauma experiences and their relation with suicidal ideation among Ohio Army National Guard Soldiers". Prescott, M. Society for Epidemiologic Research on June 18, 2013.

h. "Mediatory Effects of Civilian Social Support on the Progression of Deployment-Related PTSD". Biehn, T. University of Toledo Research Day on April 12, 2013.

i. "Civilian Social Support and PTSD". Biehn, T. Society of Biological Psychiatry on May 16, 2013.

j. "Association of Spirituality and Mental Health in an Ohio Army National Guard Sample". Tamburrino M. American Psychiatric Association on May 18, 2013.

k. "Genetic findings using medium throughput Goldengate assays". King, T. Society of Biological Psychiatry on May 16, 2013

l. "Relations Between the Underlying Dimensions of PTSD and Major Depression Using an Epidemiological Survey of Deployed Ohio National Guard Soldiers". Biehn T. American Psychiatric Association on May 18, 2013

CONCLUSION

Since 2008, the objective of the Ohio Army National Guard Mental Health Initiative (OHARNG MHI) has been to evaluate the relationships between resilience and risk factors, both cross-sectionally and longitudinally, before, during, and after deployment. The project has, from its inception, sought to integrate epidemiological data with measures of underlying biological mechanisms and now clinical trials (Blow et al.) of interventions aimed at mitigating psychopathology and enhancing resilience. The OHARNG MHI has an established track record and solid infrastructure in place to address substantive questions in both basic and applied science.

The OHARNG MHI has an established track record and solid infrastructure in place to address substantive questions in both basic and applied science. Critically, the OHARNG MHI study telephone interview methodology has been clinically validated with the in-person subsample (n=500) using gold-standard structured interviews (i.e. SCID, CAPS) delivered by trained clinicians (Prescott, et al. 2013). The OHARNG MHI has documented relationships between National Guard-specific pre-, peri- and post-deployment factors and risk or resilience in relation to DSM-IV Axis I disorders, including PTSD (Goldmann, et al. 2012), alcohol abuse (Orr, et al. under preparation), and risk-taking behavior (Hoggatt, et al. under review). We have documented susceptibility factors and correlates for the development of depression and suicidal ideation, and have identified mental health consequences of cigarette smoking. In addition, we have contributed to a further understanding of psychometrics such as the factor structure of major depression symptoms (Elhai, et al. 2012) and the relationships between underlying dimensions of PTSD and Major Depression (Biehn, et al. 2013).

More specifically, our group has demonstrated that protection against PTSD is associated with potentially modifiable pre-, peri-, and post-deployment factors including military preparedness, unit-support, and post-deployment support protect against PTSD. Additionally, we found that PTSD is associated with suicidal ideation, HIV-risk behavior (Marshall, et al. 2013) and risky driving (Hoggatt, et al. under review). Studying depression with a life course perspective, we have found that childhood abuse (Rudenstein, et al. under preparation) and adult smoking are associated with elevated risk, while depression in turn is associated with HIV risk behavior (Marshall, et al. 2013) and risky driving (Hoggatt, et al. under review). We have found that incident alcohol abuse risk is associated with coincident PTSD and depression (Marshall, et al. 2012) and deployment to a combat setting (Elhai, et al. 2012), while protection is associated with post-deployment support, being married and being female (Orr, et al. under preparation). In addition, we found that only 20% of those with an alcohol use disorder were reported past-year use of mental health services, compared to 43% of those with depression, and 61% of those with PTSD. We have examined factors associated with suicidality, and found that suicidal ideation is robustly predicted by PTSD comorbidity (Calabrese, et al., 2011). Additionally, we demonstrated longitudinal associations between incident suicidal ideation and prior smoking (Goodwin, et al. 2012) as well as alcohol dependence (Cohen, et al. under preparation). Finally, this well characterized representative cohort allowed us to meaningfully contribute to rapidly developing field of PTSD genetics by

replicating three prior genetic findings regarding sex-specific impact of the PAC1 receptor gene, and gene-environment interaction findings for FKBP5 and SLC6A4 as well as investigation of novel genetic targets (King, et al. 2012).

On July 26, 2013 the OHARNG MHI investigative team submitted an application to the Joint Warfighter's Research Program to resume Wave 5 data collection. With additional funding, the OHARNG MHI will be able to characterize trajectories of posttraumatic psychopathology and their stability over a longer period of time than previously possible. We will work to delineate the relative importance of military and civilian experiences, in an attempt to identify potentially modifiable risk factors. Importantly, using our existing genetics sample, we will investigate genetic factors associated with trajectories of risk and resilience, leveraging data observed with our custom 4600 SNPS Illumina chip to examine trajectories as phenotypic markers. Building upon our prior work we plan to study alcohol misuse and its relationship to resilience and posttraumatic psychopathology and their trajectories. Understanding trajectories of psychological health among these troops is of great importance to their long-term health and resilience. It will also inform planning for their health care delivery.

Most importantly, this project has provided the military with novel, long-term, prospective data on the National Guard, traditionally an understudied military population. Over the years of this project, this investigative team has developed especially close working relationships then COL John Harris now BG General aTAG for the Ohio Army Guard, Major General TAG Ohio Guard Gregory Wayt (2006-2011; now retired), Major General Ashenhurst Deborah The TAG for the Ohio Guard, Major James Sizemore (Chaplain between 2006-2009, now retired, who co-authored the study's first data-paper with Calabrese et al 2011), Jeremy Kaufmann, PhD (Ohio Guard Director of Psychological Health (member, Scientific Advisory Board), COL Julie Blike (Director State Family Readiness & Warrior Support Programs Deputy Commander Resilience), CPT Sephan Frazier (Risk Reduction, and Suicide Prevention Program Manager), and Everett Wade (J1 IM Branch Chief). This project has in the past and will continue in the future to provide the TAG, aTAG, and commanders of the Ohio Guard with useful, pragmatic information immediately relevant to the training of men and women in the Ohio Reserve Component. The leadership of the OHARNG recognizes and appreciates the commitment on the part of this investigative team to design and conduct research deemed pragmatically relevant to the specific translational needs of the Ohio Guard. The leadership of the Ohio National Guard is in support of and encourages the OHARNG MHI's future initiatives listed below.

FUTURE OHARNG MHI INITIATIVES:

1. OHARNG Mental Health Initiative – A Continuation and Expansion to a Second State

    On March 7, 2013, Dr. Calabrese discussed the future of this initiative with the leadership of the Ohio Army National Guard including the following: Major General Deborah Ashenhurst, 'The Adjutant General' of the Ohio National

Guard; Brigadier General John Harris, 'The Assistant Adjutant General' for the Army; COL Julie Blike, Director State Family Readiness & Warrior Support Programs Deputy Commander; Major Jeremiah Gladden, Ohio Deputy State Surgeon; and Jeremy Kaufman, PhD, Director of Psychological Health. The leadership supported this potential expansion of the project to a secondary platform and suggested the investigative team select a second state recognized as being geographically and ethnically distinct from the state of Ohio.

The secondary platform will employ methodology which is virtually identical to that employed in Ohio to study trajectories of mental health sequelae, as well as resilience and risk factors, following exposure to trauma in two separate distinct cohorts. The secondary platform would also be created with a random representative cohort of at least 3,000 National Guard members. Consistent with the methodology employed in Ohio, annual participant follow-up will take place (N=2,000) and the sample would be replenished with a dynamic cohort as needed starting in Wave 2. The data obtained from the second cohort will have four annual waves (Waves 1-4).

2. Expand the focus from Title 32 (National Guard) to Title 10 (Reserve Components)

   Since the project's inception, the focus has been on the health and well being of the Ohio Army National Guard members. Since the beginning of OIF and OEF reserve component members have become an increasingly large and important part of the overall military force. Given high demands on reserve component personnel and their increased centrality to the overall force, it is critical that we better understand the psychological characteristics and challenges that potentially impact the psychological health and resilience of Reserve Component members.

3. Sexual violence among National Guard members
   The TAG Ashenhurst has advised the investigative team to move forward with a project focusing on sexual violence in the National Guard based on Kate Walsh's manuscript entitled "Unit Support Protects Against Sexual Harassment and Assault in the Military"(Walsh, et al. under review). The team has begun a pre-proposal for submission to the BAA FY14.

4. Chronic Pain among National Guard members
   Dr. Gretchen Tietjan and Dr. Marijo Tamburrino at the University of Toledo have prepared a grant application entitled "Development and Pilot Trial of an Internet Based Chronic Pain Self Management Program for Members of the Ohio Army National Guard" for submission to the National Center for Complementary and Alternative Medicine.

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TABLE 1: MANUSCRIPTS PUBLISHED, IN PRESS, UNDER REVIEW, AND UNDER PREPARATION

Title	First Author	Date	Status
1. PTSD comorbidity and suicidal ideation associated with PTSD within the Ohio Army National Guard – **Journal of Clinical Psychiatry** • 61.7% of guard members with PTSD in the last year had at least one other psychopathology; 20.2% has at least two other co-occurring conditions. • The most common co-occurring psychopathology was depression. • While those with PTSD overall were 5.4 (95%CI 3.8 – 7.5) times more likely to report suicidality than those without PTSD • Those who had at least two additional conditions along with PTSD were 7.5 (95%CI 3.0 – 18.3) times more likely to report suicidal ideation at some point in their lifetime than those with PTSD alone.	**Joseph R. Calabrese, MD**	**August 2011**	**Published**
2. Potentially Modifiable Pre-, Peri-, and Post-deployment Characteristics Associated With Deployment-Related Posttraumatic Stress Disorder Among Ohio Army National Guard Soldiers - **Annals of Epidemiology** • Results show that factors throughout the life course of deployment in particular, post-deployment support may influence the development of PTSD. • These results suggest that the development of suitable post deployment support opportunities may be centrally important in mitigating the psychological consequences of war.	**Emily Goldmann, PhD**	**February 2012**	**Published**
3. Coincident posttraumatic stress disorder and depression predict alcohol abuse during and after deployment among Army National Guard soldiers – **Drug and Alcohol** • Coincident depression and PTSD were predictive of developing peri-/post-deployment alcohol	**Brandon D. Marshall, PhD**	**August 2012**	**Published**

abuse, and thus may constitute an etiologic pathway through which deployment-related exposures increase the risk of alcohol-related problems.			
4. The factor structure of major depression symptoms: A test of four competing models using the Patient Health Questionnaire-9 – **Psychiatry Research** • Results demonstrated greater support for the two-factor models of depression than for the one-factor model.	**Jon D. Elhai, PhD**	**October 2012**	**Published**
5. Relations between the underlying dimensions of PTSD and major depression using an epidemiological survey of deployed Ohio National Guard soldiers – **Journal of Affective Disorders** • Results demonstrated that both PTSD's dysphoria and hyperarousal factors were more related to depression's somatic than non-somatic factor • PTSD's dysphoria was more related to somatic depression than PTSD's hyperarousal factor. • Given PTSD's substantial dysphoria/distress component these results have implications for understanding the nature of PTSD's high comorbidity with depression.	**Tracy L Biehn**	**January 2013**	**Published**
6. Posttraumatic stress disorder and HIV risk behavior among Army National Guard soldiers – **Journal of Traumatic Stress** • Soldiers with PTSD may be at greater risk of HIV infection due to increased engagement in HIV risk behavior. • New onset depression following trauma mediates this relationship. • Integrated interventions to address mental health problems and reduce HIV risk behavior are in need of development and evaluation.	**Brandon D. Marshall, PhD**	**February 2013**	**Published**
7. Cigarette smoking and subsequent risk of suicidal ideation among National Guard Soldiers – **Journal of Affective Disorders** • Army National Guard soldiers who smoke have a greater risk of subsequent suicidal ideation.	**Renee D. Goodwin, PhD**	**February 2013**	**Published**

• Depression concurrent with suicidal ideation appears to explain this relationship. • If these results are replicated, screening of soldiers who smoke may be recommended as a proactive step towards mitigating the high risk of suicide in military personnel.			
8. Smoking is a predictor of depression onset among National Guard Soldiers – **Psychiatry Research** • Persistent, active smoking is associated with increased risk of incident depression at follow up. • History of smoking in the absence of current smoking at baseline was not associated with depression at follow-up.	**Renee D. Goodwin, PhD**	**April 2013**	**Published**
9. Validation of the telephone-administered PHQ-9 against the in-person administered SCID-I major depression module – **Journal of affective Disorders.** • To screen for depression effectively, results indicate use of the cardinal first two items, items representing fatigue, appetite and sleep changes with an item level cut-off point of two, and the item representing suicidal ideation with item level cut-off points of one • Total PHQ-9 scores significantly predicted SCID-I major depressive episode (MDE) and diagnosis (MDD) with moderate accuracy • The cut-off total score of 10 has the optimal balance of sensitivity and specificity compared to the other PHQ-9 scoring options	**Thomas H. Fine, MA**	**September 2013**	**Published**
10. Validation of lay-administered mental health assessments in a large Army National Guard cohort – **International Journal of Methods in Psychiatric Research** • Most commonly reported lifetime conditions were: alcohol abuse 24%, alcohol dependence 23.5%, any depressive disorder 21.4%, and PTSD 9.6%. • Telephone survey assessment for PTSD and for any depressive disorder were both highly specific [92% (SE 0.01), 83% (SE 0.02)] with moderate	**Marta R. Prescott, PhD**	**January 2013**	**In Press**

sensitivity [54% (SE 0.09), 51% (SE 0.05)] • Other psychopathologies assessed included alcohol abuse [sensitivity 40%, (SE 0.04) and specificity 80% (SE 0.02)] and alcohol dependence [sensitivity, 60% (SE 0.05) and specificity 81% (SE 0.02)].			
11. Civilian stressors are associated with post-deployment alcohol use disorders among soldiers returning from OIF and OEF – **JAMA Psychiatry** • In a model including both measures of civilian stressors and traumatic event experiences during and following combat, only civilian stressors (OR=1.86, 95% CI = 1.33-2.59) were a significant predictor of subsequent alcohol use disorder • The effects of civilian stressors were only present among persons with no prior history of alcohol use disorder	**Magdalena Cerda, DrPH**	**April 2013**	**Under Peer Review**
12. Alcohol dependence predicts incident suicidal ideation among Ohio Army National Guard Soldiers – **Journal of Clinical Psychiatry** • Both alcohol dependence and current depression are independently associated with suicidal ideation • Individuals who report depression in wave 1 are 3 times more likely to have suicidal ideation in wave 2 • Individuals with alcohol dependence in wave 1 are 3.4 times more likely to have suicidal ideation in wave 2 • Individuals with PTSD in wave 1 are 2.3 times more likely to have suicidal ideation in wave 2	**Gregory Cohen, MSW**	**May 2013**	**Under Peer Review**
13. Mental health service use in a representative sample of National Guard soldiers – **American Journal of Psychiatry** • Approximately 16% of National Guard members used mental health services during the one-year period • Among those with depression, post-traumatic	**Renee D. Goodwin, MPH, PhD**	**June 2013**	**Under Peer Review**

stress disorder, anxiety, alcohol use disorders, or suicidal ideation, 36.6% reported using services in the subsequent 12-months • Among all National Guard Soldiers, being female, Black, Hispanic, being insured and having co-morbid physical and mental health problems predicted mental health service use • Among those with mental health problems, only black race predicted mental health service use			
14. ADRB2 gene polymorphism interacts with childhood trauma in conveying risk for adult posttraumatic stress disorder (PTSD) – **Archives of General Psychiatry** • The identification of a SNP within the promoter region of ADRB2 gene associated with PTSD symptoms in interaction with childhood trauma (rs2400707, $p = 1.02 \times 10^{-5}$, significant after a Bonferroni correction, additive genotype relative risk ~1.5, controlling for level of lifetime trauma exposure • Association of rs2400707 with PTSD in interaction with childhood adversity was confirmed in an independent, predominantly female, African American cohort (Grady Trauma Project N = 2083, rs2400707 x childhood trauma interaction, $p = 5.01 \times 10^{-4}$	**Israel Liberzon, MD, PhD**	**July 2013**	**Under Peer Review**
15. Risk-taking behavior among National Guard Soldiers – **Traffic Injury Prevention.** • Drinking and driving, passing on the right, and ignoring speed limits were positively associated with a history of psychiatric disorders, deployment, deployment-related traumatic events, and combat or post-combat stressors • High self-reported psychosocial support was negatively associated with risky driving	**Katherine J. Hoggatt**	**September 2013**	**Under Peer Review**
16. Unit Support Protects Against Sexual Harassment and Assault in the Military – **Journal of Preventive Medicine** • At wave 1, 13.2% (n=198) of men and 43.5%	**Kate Walsh, PhD**	**Pending**	**Under Peer Review**

(n=74) of women reported any sexual harassment, and 1.1% (n=17) of men and 18.8% (n=32) of women reported any sexual assault during their most recent deployment. At wave 2, 13.8% (n=26) reported any harassment or assault. • Higher unit support was associated with decreased odds of sexual harassment and assault at both waves.			
17. Adverse childhood events and the risk for new onset depression and posttraumatic stress disorder among US National Guard Soldiers • A history of any childhood adversity was significantly associated with new onset depression, but not PTSD, post-deployment • The magnitude of the association between emotional maltreatment as a child and incident depression was higher than between physical abuse, or more generally, any child abuse and incident depression	**Sasha Rudenstine, PhD**	**September 2013**	**Under Preparation**
18. Lifetime substance use disorder the most common Axis I diagnosis in Army National Guard Soldiers: baseline prevalence in a longitudinal Study – **Psychiatry Research** • 66.2% of the clinical subsample had at least one DSM-IV lifetime disorder • Substance use disorders were 52.2%, follow by mood disorders (30.0%) and anxiety disorders (22.0%) • 24.8% of the clinical subsample had at least one current DSM-IV disorder • Deployed soldiers had a higher lifetime prevalence of alcohol use disorders than those never deployed (53.0% vs. 39.5%, p = 0.005) and PTSD (8.3% vs. 1.9%, p = 0.005) • Women more often had a history of mood disorders as compared to men (43.3% vs. 28.2%, p = 0.016)	**Marijo Tamburrino, MD**	**June 2013**	**Under Preparation**
19. Posttraumatic stress disorder dimensions and relations with alcohol use disorder – **Journal of**	**Tracey Biehn**	**Pending**	**Under Preparation**

Abnormal Psychology • Results of CFA indicated that a combined model of PTSD and AUD fit the data very well. Correlations between PTSD's factors and a latent AUD factor ranged from rs of .258 to .285, with PTSD's dysphoria factor demonstrating the strongest correlation.			
20. What drives non-medical prescription drug use among National Guard Soldiers	**Magdalena Cerda**	**Pending**	**Under Preparation**
21. Prevalence and Determinants of military TBI in the Ohio National Guard	**Laura Sampson**	**Pending**	**Under Preparation**
22. Longitudinal trajectories of 12-month PTSD and depression in the Ohio National Guard	**Laura Sampson**	**Pending**	**Under Preparation**
23. Type and setting of potentially traumatic events as determinants of 12-month depression in the Ohio National Guard	**Laura Sampson**	**Pending**	**Under Preparation**
24. Patterns and predictors of treatment after first onset of psychiatric disorders among Ohio National Guardsman	**David Fink**	**Pending**	**Under Preparation**
25. Onset, chronicity, and comorbidity patterns of mood and anxiety disorders in a representative sample of the Ohio National Guard	**David Fink**	**Pending**	**Under Preparation**

Research report

Relations between the underlying dimensions of PTSD and major depression using an epidemiological survey of deployed Ohio National Guard soldiers

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A B S T R A C T

Background: In the present study, the authors investigated the relationship between the underlying symptom dimensions of posttraumatic stress disorder (PTSD) and dimensions of major depressive disorder (MDD).
Method: A sample of 1266 Ohio National Guard soldiers with a history of overseas deployment participated and were administered the PTSD Checklist (assessing PTSD) and Patient Health Questionnaire-9 (assessing depression).
Results: Using confirmatory factor analysis, results demonstrated that both PTSD's dysphoria and hyperarousal factors were more related to depression's somatic than non-somatic factor. Furthermore, depression's somatic factor was more related to PTSD's dysphoria than hyperarousal factor.
Limitations: Limitations of this study include the use of self-report measures and a predominately male military sample.
Conclusions: Results indicate that PTSD's dysphoria factor is related to depression specifically by way of depression's somatic construct. Given PTSD's substantial dysphoria/distress component, these results have implications for understanding the nature of PTSD's high comorbidity with depression.

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1. Introduction

There are substantial rates of comorbidity between posttraumatic stress disorder (PTSD) and major depression. For example, the National Comorbidity Survey (NCS) found that 48–55% of individuals diagnosed with PTSD were also diagnosed with major depression in their lifetimes (Kessler et al., 1995). While the comorbidity between PTSD and depression is well established (Elhai et al., 2011a; Keane and Kaloupek, 1997), few studies have examined how the underlying dimensions of PTSD and depression are most related to each other in order to further understand the high comorbidity rates.

Several hypotheses have been proposed to explain the significant comorbidity between PTSD and major depressive disorder. We focus on two hypotheses in particular. First, several symptoms overlap between DSM-IV major depressive disorder (MDD) and PTSD (i.e., difficulties with sleep, concentration and anhedonia). As a consequence, satisfying criteria for one of these two disorders places an individual at substantial risk of being diagnosed with the other disorder merely by virtue of these overlapping symptoms (Spitzer et al., 2007). Second, there may be a shared underlying latent association behind depression and PTSD. Watson (2005) proposed that mood and anxiety disorders are defined by a higher order negative affect factor which subsumes a broad range of negative emotional states including fear, anger, and sadness. Watson argued that this higher order

factor accounts for the high rates of comorbidity among mood and anxiety disorders, such as major depression and PTSD.

Recently, researchers have investigated the overlapping symptoms hypothesis of PTSD's comorbidity. Spitzer et al. (2007) suggested that removing the overlapping PTSD–depression items should result in a more pure, less comorbid PTSD diagnostic construct. However, a study by Elhai et al. (2008) found instead that removing overlapping items had negligible effects on PTSD's comorbidity rates (after removing overlapping items, comorbidity rates dropped nominally from 54.72% to 54.41% in the NCS Replication dataset). Similar results were found in a study of military veterans by Grubaugh et al. (2010) and a study of nationally representative, trauma-exposed adolescents conducted by Ford et al. (2009). Thus symptom overlap does not seem to primarily account for the PTSD–MDD comorbidity.

The shared latent mechanism hypothesis has been investigated as well, by examining PTSD's robust, empirically supported latent factor of dysphoria that is conceptually similar to the general negative affect construct (Simms et al., 2002). We discuss the dysphoria construct more extensively below in the context of factor analysis. Factor analysis is a relatively under-utilized approach to examining issues of comorbidity between mental disorders. The use of factor analysis can help to elucidate the nature of comorbidity by examining which underlying factors of a disorder are more highly correlated with factors of another similar mental disorder. This method can be used to test the construct validity of a disorder (e.g., its uniqueness as a disorder) in a more refined manner than by examining comorbidity between crudely measured, observed diagnostic variables. Furthermore, this research is particularly timely given that a new edition of the *DSM* is currently being developed.

1.1. PTSD's factor structure

There are two models of underlying PTSD symptoms that have received substantial empirical support. One model proposed by King et al. (1998) comprises the following four intercorrelated factors: re-experiencing, effortful avoidance, emotional numbing, and hyperarousal. This model is essentially identical to *DSM-IV*'s conceptualization of PTSD except that the avoidance and numbing symptom cluster (PTSD's Criterion C) is separated into distinct avoidance and numbing factors, supported by empirical research (reviewed by Asmundson et al., 2004). The other empirically supported PTSD model is the dysphoria model proposed by Simms et al. (2002), comprising the following four intercorrelated factors: re-experiencing, avoidance, dysphoria, and hyperarousal. In this model, the numbing items are combined with three hyperarousal items (difficulties with sleep, concentration difficulties, and irritability) to form a dysphoria factor which involves symptoms of emotional distress common to mood and anxiety disorders (reviewed in Watson, 2005). In this model of PTSD, the hyperarousal factor only contains anxious-arousal items (hypervigilance and exaggerated startle response) which are more characteristic of fear based disorders. Both models have been extensively studied using confirmatory factor analysis (CFA), demonstrating good fit among different trauma exposed samples and using a variety of PTSD instruments (reviewed in Elhai and Palmieri, 2011; Yufik and Simms, 2010).

One specific research question that recent empirical studies have tested is the notion that PTSD's dysphoria factor drives PTSD's association with external measures of depression and general emotional distress. Several studies have found support for this notion (Elklit et al., 2010; Forbes et al., 2010; Simms et al., 2002). However, other studies have found that in contrast to other factors of PTSD, PTSD's dysphoria is no more related to depression and distress (Marshall et al., 2010; Miller et al., 2010). Importantly, these studies used crude, unitary measures of depression and distress rather than examining these constructs in a more refined manner to better understand the PTSD–depression relationship.

1.2. Depression's factor structure

There is less research regarding the factor structure of major depressive disorder, and the resulting factor structure often differs depending on the specific depression instrument used to assess depressive symptoms. In the present study, the Patient Health Questionnaire-9 (PHQ-9) was used to examine depression's factor structure. The PHQ-9 is a widely used self-report measure of depression and maps directly onto *DSM-IV* symptom criteria for a major depressive episode (MDE) (Kroenke et al., 2001). Although the PHQ-9 has been empirically well-researched, few studies have analyzed its factor structure using CFA. Prior studies have used exploratory factor analyses (EFA) (Cameron et al., 2008; Dum et al., 2008; Huang et al., 2006; Kalpakjian et al., 2009; Krause et al., 2010) and CFA (Baas et al., 2011; Krause et al., 2008) to assess the PHQ-9's symptom structure. Most PHQ-9 factor analytic studies either support a unidimensional depression model (Baas et al., 2011; Cameron et al., 2008; Dum et al., 2008; Kalpakjian et al., 2009) or a two-factor model of somatic and non-somatic/affective dimensions (Krause et al., 2008; 2010; Richardson and Richards, 2008).

The only study, to our knowledge, that has empirically tested several PHQ-9 depression factor models simultaneously with objective statistical criteria using CFA was a study conducted by Elhai et al. (in press). Overall, this and other studies have found the most support for a two-factor model, with one factor comprising five somatic items (sleep changes, appetite disturbances and feeling tired, difficulty concentrating and psychomotor changes) and the other factor primarily based on four non-somatic or affective items (anhedonia, depressed mood, suicidal thoughts, and feeling bad about oneself) (Elhai et al., in press; Krause et al., 2010; Richardson and Richards, 2008).

1.3. Relationship between the factor structure of depression and PTSD

Despite PTSD's high comorbidity with major depressive disorder, lacking in the literature is a more refined analysis of the PTSD–depression relationship by exploring relations between the latent factors of PTSD and MDD. In only one recent study, evidence demonstrated that PTSD's dysphoria factor was strongly related to the Center for Epidemiologic Studies-Depression Scale's (CES-D) factors of somatic problems and negative affect, indicating that the shared variance between the two comorbid disorders may be best accounted for by the dysphoria symptoms present in the PTSD diagnosis (Elhai et al., 2011b). Specifically, this study found that the PTSD dysphoria factor demonstrated a strong relationship with the CES-D's depressive affect ($r=.77$) and somatic problems ($r=.84$) factors, compared to the positive affect ($r=-.45$) and interpersonal problems ($r=.65$) factors. Although this study provides a better understanding of the relationship between the latent factors of PTSD and MDD, the CES-D is a 20-item depression instrument that does not directly map onto *DSM-IV*'s major depressive disorder criteria. Therefore, it is unknown whether those study results are generalizable to a *DSM-IV* major depression-based instrument that would be more likely used to support a MDD diagnosis.

1.4. Study aims

The purpose of the current study was to replicate and extend findings by Elhai et al. (2011b) to further examine the

relationship between the latent factors of PTSD and depression in a sample of war-exposed military veterans. At present, this is only the second known study to address the comorbidity of PTSD and depression by analysis at the latent level. The Simms et al. (2002) dysphoria model was used to model PTSD symptoms given that this model comprises a general negative affect component which is conceptually similar to depression. Krause et al.'s (2008) two-factor depression model of somatic and non-somatic factors was used to analyze the depression factor structure, given that this model has received the most empirical support (Elhai et al., in press). We used the PTSD Checklist (PCL) to measure PTSD symptoms, and the PHQ-9 to measure major depression symptoms.

We were interested in testing if the dysphoria and hyperarousal factors of PTSD were more related to depression's somatic vs. non-somatic factor. Four specific hypotheses were tested in particular. The first hypothesis was that PTSD's dysphoria factor would correlate most strongly with depression's somatic than non-somatic factor. The dysphoria factor comprises both somatic items and non-somatic items (e.g., difficulty concentrating, feeling emotionally numb). We hypothesized that dysphoria would correlate more strongly with the somatic factor of depression given that a previous study found that PTSD's dysphoria correlated more strongly with depression's somatic complaints factor (Elhai et al., 2011b). The second hypothesis was that the two-item PTSD hyperarousal factor (i.e., exaggerated startle response, hypervigilance) would correlate more strongly with MDD's somatic than non-somatic factor given that these items are somatic in nature. However, in Hypothesis 3, we expected that depression's somatic factor would more strongly correlate with PTSD's dysphoria factor than with the hyperarousal factor given that the dysphoria factor contains more somatic-related items (PTSD items D1–D3). Finally, as our fourth hypothesis, we expected that neither re-experiencing nor avoidance factors of PTSD would be differentially related to the somatic or non-somatic factors of depression, given the lack of conceptual similarities between these constructs.

2. Method

2.1. Participants and procedure

The present study was part of the Ohio Army National Guard Mental Health Initiative (OHARNG MHI), a longitudinal prospective study of mental health among National Guard soldiers in Ohio. All members of the Ohio National Guard who served between July 2008 and February 2009 were invited to participate in the telephone interview portion of the study. There were 12,225 Guard members with a valid mailing address who were invited to participate (345 individuals were excluded for having no mailing address). Among the pool of potential subjects, 1013 (8.3%) declined to participate, 1130 (10.1%) did not have a telephone number listed with the Guard, and 3568 (31.8%) did not have a correct or working phone number. Among the remaining 6514 Guard members (58.1%), the following individuals were excluded: 187 (2.8%) based on the age eligibility restrictions, 1364 (20.9%) declined to participate, 31 (.4%) for having English language or hearing difficulties, and 2316 (35.5%) for not being contacted before the cohort was closed to new recruitment. Of the remaining 2616 subjects, one subject was excluded for missing as many as six items on the PHQ-9, leaving 2615 participants. Finally, we only included participants who reported being deployed and further reported a deployment related trauma, leaving an effective dataset of 1266.

Study enrollment began in November 2008 and ended in November 2009. The National Guard Bureau, Office of Human

Research Protections of the U.S. Army Medical Research and Materiel Command, along with the institutional review boards of University Hospitals Case Medical Center, University of Toledo, and Columbia University, approved the study with written informed consent waived in lieu of verbal consent by telephone.

Among the 1266 remaining subjects, the average age of participants was 33 years ($SD=8.81$) and ranged from 18 to 60 years. The majority of participants were male ($n=1144$, 90.4%) and identified their racial background as primarily Caucasian ($n=1127$, 89.0%) or African–American ($n=81$, 6.4%). Only 16 participants identified themselves as Hispanic (1.3%). The majority of participants had at a minimum received a high school diploma or its equivalent ($n=1260$, 99.5%). Many had attended some college or technical training ($n=636$, 50.2%) or graduated from college ($n=243$, 19.2%). There were 873 participants working full-time (69.0%), 103 participants working part-time (8.1%), 185 unemployed (14.6%), and 80 who were of student status (6.3%). There were 333 participants (26.3%) who had a household income greater than $80,000. Income of $20,000 or less was reported by 84 participants (6.6%), between $20,001 and $40,000 by 276 respondents (21.8%), $40,001 to $60,000 by 311 participants (24.6%), and between $60,001 and $80,000 by 236 (18.6%). The average length of time participants served in the military was 12.7 years ($SD=7.81$). All participants had deployed at least once, with the average number of deployments being 2.02 ($SD=1.76$). For the majority of participants ($n=742$, 58.6%), the most recent deployment was in support of Operation Iraqi Freedom (OIF) or Operation Enduring Freedom (OEF). There were 503 (39.7%) who most recently deployed to an area of non-conflict.

The most prevalent traumatic events experienced by participants were exposure to combat ($n=999$, 78.9%), sudden and unexpected death of a loved one or close friend ($n=874$, 69.0%), witnessing someone being killed or injured ($n=968$, 55.1%), and witnessing severe human suffering ($n=598$, 47.2%). There were 240 participants (19.0%) who reported that receiving incoming hostile fire was their worst deployment related trauma. The other most frequently nominated worst deployment-related traumas included experiencing combat or exposure to a war zone ($n=87$, 6.9%), and experiencing a sudden death of a close friend or loved one ($n=69$, 5.5%).

2.2. Instrumentation

2.2.1. Computer-assisted telephone interview (CATI)

A CATI was conducted for all participants by trained professionals at the survey research firm Abt SRBI, Inc., to assess demographic characteristics and mental health functioning using standardized questionnaires.

2.2.2. PHQ-9

Participants completed the PHQ-9 (Spitzer et al., 1994). Traditionally, the PHQ-9 measures depression symptoms over the previous two weeks based on the *DSM-IV* major depressive episode symptom criteria, but for this study, the instructions were modified in order to query depression symptoms over the course of the respondent's lifetime, as done by Cannon et al. (2007). The PHQ-9 uses a Likert-type scale with four response options ranging from 0="*Not at all*" to 3="*Nearly every day*" to assess symptom severity. A study by Kroenke et al. (2001) examined the validity of using the PHQ-9 to detect and assess for depression, and found that internal consistency ranged from .86 to .89. Diagnostic validity was demonstrated in detecting an MDD diagnosis based on structured diagnostic interviews. Lastly, construct validity was reflected in the association of PHQ-9 severity scores and measures of functional

status, number of disability days and difficulties based on symptoms (Kroenke et al., 2001).

2.2.3. PCL-C

Participants also completed the PTSD Checklist – Civilian Version (PCL-C). The PCL-C was adapted so that participants were asked to anchor their PTSD ratings to one's self-nominated worst deployment trauma. The PCL is a self-report measure which maps onto the *DSM-IV* symptom criteria for PTSD. There are 17 symptoms assessed by the PCL, and respondents indicate how distressed they were by each symptom over the past month by rating items on a five-point Likert-type scale (1 = "*not at all*" to 5 = "*extremely*"); however, in our study we assessed lifetime symptoms since the worst trauma. The PCL has demonstrated adequate reliability ($\alpha = .94$; test–retest $r = .88$) in various trauma-exposed populations (Ruggiero et al., 2003), and total scores were found to highly correlate (r range $= .8 - .9$) with those from structured PTSD diagnostic interviews in military veterans (Forbes et al., 2001). The psychometric properties of the PCL are reviewed in articles by McDonald and Calhoun (2010) and Wilkins et al. (2011).

2.3. Analysis

There were nominal amounts of missing items from the PCL and PHQ measures. There were 1243 complete cases (98.2%) for the PCL and 1240 complete cases from the PHQ (97.9%). Missing data were estimated with multiple imputation procedures using an iterative Markov chain Monte Carlo method with the Gibbs Sampler procedure (in SPSS's Version 17 Missing Value Analysis software) to estimate missing item-level PCL and PHQ data, generated across 10 imputed datasets.

The data were screened for univariate and multivariate non-normality. There were several PCL and PHQ items with skewness and kurtosis values greater than 2.0, which indicated a non-normal univariate distribution. Further, Mardia's multivariate skewness and kurtosis tests indicated a non-normal multivariate distribution (p's $< .001$).

All CFA analyses were conducted using the Mplus 6.1 software, averaging parameter estimates across the 10 imputed datasets. Error covariances were fixed to zero, and factor variances were fixed to 1 to scale the factors within a model. All tests were two-tailed, with alpha set at .05. Goodness of fit indices are reported below, including the comparative fit index (CFI), Tucker Lewis Index (TLI), root mean square error of approximation (RMSEA) and standardized root mean square residual (SRMR). Models fitting very well (or adequately) are indicated by CFI and TLI $\geq .95$ (.90–.94), RMSEA $\leq .06$ (.07 − .08), SRMR $\leq .08$ (.09–.10) (Hu and Bentler, 1999).

CFA analyses for the PCL were conducted using maximum likelihood estimation with a mean-adjusted chi-square (MLM) (the Satorra-Bentler chi-square value), which is robust to non-normality (Satorra and Bentler, 2001). In the first CFA, we examined PTSD's dysphoria model, with PCL items 1–5 specified to load onto the re-experiencing factor, PCL items 6 and 7 on the avoidance factor, PCL items 8–15 on the dysphoria factor, and PCL items 16 and 17 on the hyperarousal factor. The PCL items were treated as continuously scaled items. Next, Krause's depression model was examined using the PHQ items. PHQ items 1, 2, 6, and 9 were specified to load onto the non-somatic factor, and PHQ items 3, 4, 5, 7, and 8 on the somatic factor. The PHQ items were also treated as continuously scaled items, using MLM estimation. A CFA was then conducted to examine the combined PTSD dysphoria and depression model, with all factors allowed to correlate.

Wald's chi-square test of parameter constraints was used, which tests the null hypothesis that the difference between two correlations would be zero; we used an alpha level of .01 to control for Type I error. These analyses were conducted to determine if specific PTSD dysphoria model factors were more highly correlated with either the non-somatic or somatic factors of the depression model. Specifically, we tested whether the PTSD's dysphoria factor was more related to depression's somatic than non-somatic factor (Hypothesis 1). Likewise, we next tested whether the PTSD's hyperarousal factor was more related to depression's somatic than non-somatic factor (Hypothesis 2). Additionally, we tested whether depression's somatic factor would be more related to PTSD's dysphoria than hyperarousal factor (Hypothesis 3). Furthermore, we tested whether PTSD's re-experiencing and avoidance factors (separately) were differentially related to depression's somatic vs. non-somatic factors (Hypothesis 4).

3. Results

The average PHQ total score among participants was 5.85 ($SD = 6.18$), and the average PCL score was 29.86 ($SD = 14.60$). A PCL cutoff score of 50 in military veterans best discriminates between those with and without PTSD (McDonald and Calhoun, 2010). Kroenke et al. (2001) reported that PHQ-9 scores greater than 10 result in a sensitivity of 88% and specificity of 88% for detecting major depressive disorder.

CFA results from the PTSD dysphoria model indicate that the model fit well, S–B $\chi^2(113, N = 1266) = 569.53$, $p < .001$, CFI $= .95$, TLI $= .93$, RMSEA $= .06$, SRMR $= .03$. Similar well-fitting results were obtained from Krause's 2-factor depression model, $\chi^2(26) = 131.93$, $p < .001$, CFI $= .95$, TLI $= .94$, RMSEA $= .06$, SRMR $= .04$. The 6-factor combined model also fit the data well, $\chi^2(284, N = 1266) = 1115.407$, $p < .001$, CFI $= .93$, TLI $= .93$, RMSEA $= .05$, SRMR $= .04$.

Wald's tests of parameter constraints were conducted in order to test our hypotheses regarding the differential relationship between the somatic and non-somatic factors of depression with the four PTSD factors. Results indicated that PTSD's dysphoria factor was more strongly correlated with depression's somatic factor ($r = .69$) than with the non-somatic factor ($r = .59$), $\chi^2(1) = 3.323$, $p < .048$, as expected (Hypothesis 1). PTSD's hyperarousal factor was also more correlated with depression's somatic factor ($r = .51$) than with the non-somatic factor ($r = .34$), $\chi^2(1) = 21.731$, $p < .001$ (Hypothesis 2) (Table 1).

Next, to assess Hypothesis 3, we assessed whether depression's somatic factor was more related to PTSD's dysphoria than hyperarousal factor. Results indicated that the depression somatic factor was more strongly correlated with PTSD's dysphoria ($r = .69$) than with hyperarousal ($r = .51$), $\chi^2(1) = 64.482$, $p < .001$ (see Table 2).

Table 1
Correlations between somatic vs. non-somatic factors with PTSD factors.

Correlation between factors	r Value	Wald chi-square
Re-experiencing and somatic	$r = .544$	$\chi^2(1) = 3.306$, $p = .069$
Re-experiencing and non-somatic	$r = .459$	
Avoidance and somatic	$r = .537$	$\chi^2(1) = 6.502$, $p = .011$
Avoidance and non-somatic	$r = .425$	
Dysphoria and somatic	$r = .689$	$\chi^2(1) = 3.323$, $p = .048$
Dysphoria and non-somatic	$r = .592$	
Hyperarousal and somatic	$r = .505$	$\chi^2(1) = 21.731$, $p < .001$
Hyperarousal and non-somatic	$r = .337$	

Table 2
Correlations for the Somatic factor with Dysphoria and Avoidance.

Correlation between factors	*r* Value	Wald Chi-Square
Somatic and dysphoria	$r=.689$	$\chi^2 (1)=64.482, p<.001$
Somatic and avoidance	$r=.537$	
Somatic and dysphoria	$r=.689$	$\chi^2 (1)=53.330, p<.001$
Somatic and hyperarousal	$r=.505$	

Table 3
Correlations among PTSD and depression factors.

Factor	1	2	3	4	5	6
Re-experiencing	–					
Avoidance	.898	–				
Dysphoria	.846	.837	–			
Hyperarousal	.772	.717	.740	–		
Somatic	.544	.537	.689	.505	–	
Non-Somatic	.459	.425	.592	.337	.862	–

Unexpectedly, in contrast to Hypothesis 4, the PTSD's avoidance factor was more strongly correlated with depression's somatic factor ($r=.54$) than to the non-somatic factor ($r=.425$), $\chi^2(1)=6.502$, $p<.011$.

4. Discussion

The purpose of this study was to clarify the nature of the comorbid relationship between depression and PTSD by examining the relationships between one disorder's latent factors with those of the other disorder's latent factors. It was hypothesized that PTSD's dysphoria factor would be more related to depression's somatic than non-somatic factor (Hypothesis 1), and that PTSD's hyperarousal factor would correlate more strongly with depression's somatic than non-somatic factor (Hypothesis 2). Further, it was hypothesized that depression's somatic factor would be more related to PTSD's dysphoria than hyperarousal factor (Hypothesis 3), and that PTSD's re-experiencing and avoidance would not be differentially related to depression's somatic or non-somatic factors (Hypothesis 4). Results confirmed that despite PTSD's dysphoria factor evidencing a large relationship with non-somatic aspects of major depressive disorder ($r=.59$), dysphoria was significantly more related to somatic depression ($r=.69$). As hypothesized, PTSD's hyperarousal factor was also more strongly correlated with depression's somatic than non-somatic factor. However, hyperarousal was not as strongly correlated with the somatic factor as dysphoria was (Table 3).

Previous research has found mixed support for the notion that PTSD's dysphoria is especially related to depression and general emotional distress. While some studies (Elklit et al., 2010; Forbes et al., 2010; Simms et al., 2002) have found that PTSD's dysphoria is uniquely related to emotional distress, other studies have failed to replicate that finding (Marshall et al., 2010; Miller et al., 2010). The present study clarifies these findings by more precisely analyzing depression not as a crude single variable but rather by analyzing its underlying factors. Thus perhaps mixed findings for dysphoria's external relationships resulted because depression and/or general emotional distress were analyzed as global external variables.

Rather based on our findings, analyzing depression based on its subcomponents, we find that PTSD's dysphoria is related to depression specifically by way of depression's somatic construct. Our findings corroborate those of a recent factor analytic study

which examined the combined symptom structure of PTSD and depression symptoms. In that paper, Elhai et al. (2011b) also found that PTSD's dysphoria factor was more related to somatic symptoms of depression. It is possible that the shared somatic components to both PTSD and depression could account for the comorbidity between depression and PTSD. Perhaps PTSD is so highly comorbid with major depressive disorder because of the shared somatic component between these disorders.

Although PTSD's dysphoria factor shares two symptoms with the PHQ-9's somatic factor (sleep and concentration difficulties), which could account for its substantial relationship, the dysphoria factor has several other symptoms that are not shared by the somatic factor. Furthermore, it should be noted that research demonstrates that symptom overlap between PTSD and major depressive disorder is not solely responsible for the high rates of comorbidity between these two disorders (Elhai et al., 2008; Ford et al., 2009; Grubaugh et al., 2010).

The hypothesis that the somatic and non-somatic factors of depression would not be differentially related to either PTSD's re-experiencing or avoidance factors was not supported. Specifically, results indicated that depression's somatic factor was significantly more correlated with avoidance than the non-somatic factor was. It may be that individuals who use avoidance as a coping mechanism exhibit more somatic signs of distress (Morina et al., 2010). Avoidance in fact is considered a maladaptive emotion regulation strategy that leads to an increase in PTSD symptoms—especially physiological (somatic) manifestations of fear (Foa and Kozak, 1986).

Limitations of this study include using self-report instruments (in particular, by telephone) to assess PTSD and depression severity. Thus the limitations that are inherent in using self-report measures apply to this study, including potential problems with response validity, social desirability, memory recall, etc. Additionally, most respondents were men, and thus women were underrepresented. Furthermore, we assessed lifetime symptoms of depression and PTSD and thus we cannot generalize these findings to current assessment of PTSD and depression. Also, the relatively low mean scores on the PHQ-9 and PCL indicate relatively modest MDD and PTSD severity among respondents. Thus, the results of this study may not generalize to a sample of patients with more severe depression and PTSD. Finally, the results may not generalize to civilian trauma-exposed samples. Future studies should test these research questions using structured diagnostic interviews. Future studies should also attempt to use a more diverse sample exposed to a wider range of traumatic events.

Conflict of interest
No conflict declared.

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Posttraumatic Stress Disorder, Depression, and HIV Risk Behavior Among Ohio Army National Guard Soldiers

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We examined the relationship between posttraumatic stress disorder (PTSD), major depressive disorder (MDD), and human immunodeficiency virus (HIV) risk behavior among the Ohio Army National Guard (OHARNG). We analyzed data collected from a sample of OHARNG enlisted between June 2008 and February 2009. Participants completed interviews assessing HIV risk activities defined by the Behavioral Risk Factor Surveillance System, and were screened for PTSD and MDD based on DSM-IV criteria according to the *Diagnostic and Statistical Manual of Mental Disorders* (4th ed., *DSM-IV*; American Psychiatric Association, 1994). Logistic regression was used to examine the independent and combined effects of PTSD and MDD on past-year HIV risk behavior. Of 2,259 participants, 142 (6.3%) reported at least 1 past-year HIV risk behavior. In adjusted models, relative to soldiers with neither disorder, screening positive for MDD only was associated with HIV risk behavior (adjusted odds ratio [*AOR*] = 2.33, 95% CI = [1.15, 4.71]), whereas PTSD was not significant (*AOR* = 1.60, 95% CI = [0.80, 3.20]). Participants with both PTSD and depression were most likely to report HIV risk behavior (*AOR* = 2.75, 95% CI = [1.06, 7.11]). Soldiers with PTSD and MDD may be at greater risk for HIV infection due to increased engagement in HIV risk behavior. Integrated interventions to address mental health problems and reduce HIV risk behavior are in need of development and evaluation.

Posttraumatic stress disorder (PTSD) has long been recognized as a debilitating condition that adversely affects physical and psychological health (Breslau, Davis, Peterson, & Schultz, 1997; Davidson, Hughes, Blazer, & George, 1991; Zatzick et al., 1997). The development of PTSD is associated with a variety of health behaviors (e.g., smoking, alcohol and substance use, physical inactivity) that increase the risk of morbidity and mortality (Breslau, Davis, & Schultz, 2003; Buckley, Mozley, Bedard, Dewulf, & Greif, 2004;

Schnurr & Spiro, 1999). A growing body of literature has also shown that persons who develop PTSD following exposure to trauma are more likely to participate in HIV risk behaviors (Brief et al., 2004). For example, a lifetime occurrence of PTSD has been associated with recent engagement in receptive anal intercourse and sex work among women prisoners (Hutton et al., 2001). A study of women who had experienced intimate partner violence (IPV) demonstrated that IPV-related PTSD was significantly associated with a composite measure of sexual risk behavior, and was particularly elevated among women with avoidance and numbing symptoms (Cavanaugh, Hansen, & Sullivan, 2010). Similar results have been reported among women seeking emergency care in New York City (El-Bassel, Gilbert, Vinocur, Chang, & Wu, 2011). Although fewer studies have examined the relationship between PTSD and HIV risk among men, some evidence indicates that PTSD increases the risk of unprotected anal intercourse in men who have sex with men (Reisner, Mimiaga, Safren, & Mayer, 2009).

Depression is also widely reported as a risk factor for engagement in HIV risk behavior in the general and at-risk populations (Alegría et al., 1994; Lehrer, Shrier, Gortmaker, & Buka,

2006; Perdue, Hagan, Thiede, & Valleroy, 2003; Williams & Latkin, 2005). Despite the high prevalence of mental health co-morbidities in many populations affected by HIV, research has typically focused on the independent effects of PTSD and depression in people living with or at risk for the disease (Boarts, Sledjeski, Bogart, & Delahanty, 2006). Several authors have examined the influence of comorbid conditions on adherence to HIV therapy, with two studies suggesting that depression plays a more important role in poor adherence than PTSD (Sledjeski, Delahanty, & Bogart, 2005; Vranceanu et al., 2008). Although some evidence suggests that HIV risk behaviors are particularly common among persons experiencing co-occurring depression and PTSD (Holmes, Foa, & Sammel, 2005; Plotzker, Metzger, & Holmes, 2007), these studies have focused on persons with childhood abuse histories. Therefore, more research is required to determine the unique and combined contributions of PTSD and depression on risk behavior in other populations at risk for HIV.

The objective of this study was to examine whether depression and PTSD were associated with increased engagement in HIV risk behavior among a sample of Ohio Army National Guard (OHARNG) soldiers. We also sought to determine whether soldiers with both disorders were more likely to report HIV risk behavior compared to participants reporting one or neither conditions. Although studies of active U.S. army personnel and armed forces in other countries have investigated HIV prevalence and risk factors for HIV infection including PTSD (Anastario et al., 2011; Levin et al., 1995; Tavarez, Chun, & Anastario, 2011), to our knowledge no studies have examined the relationships between depression, PTSD, and HIV risk behavior in soldiers of the U.S. National Guard. Given the high prevalence of trauma exposure and subsequent PTSD among National Guard soldiers (Calabrese et al., 2011; Kehle et al., 2011), elucidating the relationships between mental health problems and HIV risk behavior has important implications for the development of effective HIV prevention services for military personnel.

Method

Participants and Procedure

Between November 2008 and November 2009, OHARNG soldiers were recruited to participate in the OHARNG Mental Health Initiative. For the present study, all enlisted soldiers between June 2008 and February 2009 with a current address (12,225) were mailed a letter explaining the study's objectives and consenting procedures along with a prepaid opt-out card. We excluded 1,013 (8.3%) who returned an opt-out card, 1,130 (9.2%) who did not have a telephone number listed with the Guard, and 3,568 (29.2%) who had an incorrect telephone number. Of the 6,514 participants remaining, 1,364 (20.9%) refused to participate, 218 (3.3%) were excluded for other reasons (i.e., were deceased, did not speak English, had hearing problems,

or were retired), and 2,316 (35.6%) were not contacted before the cohort closed. Thus, the eligible sample was 2,616.

To examine the effect of PTSD and new onset MDD after experiencing a qualifying trauma, we used timing of symptom onset data to exclude participants who reported having depressive symptoms prior to the date of experiencing a Criterion A stressor ($n = 39$). We also excluded participants for whom the timing of onset of the trauma and depression could not be differentiated ($n = 44$), or who were missing the timing of the trauma or onset of PTSD and MDD symptoms ($n = 22$). We further excluded 141 participants who had never experienced a qualifying traumatic event, and 111 participants who had non-responses to any of the model confounding variables of interest (see below). Therefore, the final sample was $N = 2,259$, of whom, the majority were male (86.0%), White (88.1%), and less than 35 years of age (64.7%).

Computer-assisted telephone interviewing (CATI) was used to collect a wide array of information regarding sociodemographic characteristics, risk behaviors, military history, deployment and combat experiences, and past and present psychopathological symptoms. Interviews took approximately 60 minutes to complete and all participants were compensated for their time.

The study received a certificate of confidentiality from the National Institutes of Health, and the study protocol was approved by the Institutional Review Boards of University Hospitals Case Medical Center, University of Toledo, and Columbia University. The study was also approved by the Human Research Protection Office (HRPO), Office of Research Protections (ORP), and the U.S. Army Medical Research & Materiel Command (USAMRMC) of the U.S. Department of Defense. Verbal informed consent was obtained from all participants.

Measures

HIV risk. The dependent variable for this analysis was self-reported participation in HIV risk behavior(s) in the past year (yes vs. no). To define this variable, we used a standardized set of core questions from the Behavioral Risk Factor Surveillance System (BRFSS), a U.S. Centers for Disease Control and Prevention (CDC)-supported general population survey that includes measures of HIV/STD risk behaviors (Centers for Disease Control and Prevention, 2011). Core items included in the HIV/acquired immunodeficiency syndrome (AIDS) section of the BRFSS were developed by a 1997 CDC working group and were chosen after extensive cognitive laboratory testing and field piloting (Rietmeijer, Lansky, Anderson, & Fichtner, 2001). To assess HIV risk behaviors, participants were asked whether they had engaged in any of the following in the past year: (a) used intravenous drugs, (b) been treated for a sexually transmitted or venereal disease, (c) given or received money or drugs in exchange for sex, and (d) had anal sex without a condom. To be consistent with BRFSS methodology and with previously published studies using this measure (Bensley, Van Eenwyk, & Simmons, 2000; Link, Battaglia, Frankel, Osborn,

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& Mokdad, 2006; Wen, Balluz, & Town, 2012), participants were informed that they did not have to identify which risk(s) they had practiced in the past year. All participants provided a yes or no answer to the question (no nonresponses or refusals were recorded).

Psychiatric symptoms. The primary independent variables of interest were screening positive for PTSD and major depressive disorder (MDD), each based on *DSM-IV* criteria. Specifically, a positive screen for PTSD was assessed using the PTSD Checklist-Civilian Version (PCL-C), modified to include questions that assessed *DSM-IV* diagnostic Criteria A2, E, and F (Blake et al., 1995). Thus, participants screening positive for PTSD must have met all *DSM-IV* criteria related to a specific traumatic event: been exposed to a Criterion A stressor (e.g., a traumatic event involving actual or threatened death or serious injury), had at least one intrusion symptom (e.g., recurrent distressing recollections or dreams of the event), had at least three symptoms of avoidance (e.g., avoiding activities, places, or people associated with the trauma), and had at least two hyperarousal symptoms (e.g., difficulty falling asleep, hypervigilance). Based on questions that assessed duration, symptoms must also have lasted for at least a month. Participants must also have reported that symptoms caused significant social or functional impairment (e.g., very difficult to perform tasks at work, at home, or get along with others). The PCL-C has been found to be a reliable and valid instrument in both general and military personnel populations (Blanchard, Jones-Alexander, Buckley, & Forneris, 1996; Maguen et al., 2010). We assessed MDD using the Primary Care Evaluation of Mental Health Disorders Patient Health Questionnaire-9 (PHQ-9; Kroenke & Spitzer, 2002; Kroenke, Spitzer, & Williams, 2001). To screen positive for MDD, a participant had to score ≥5 of nine symptoms on the PHQ-9, and these symptoms had to occur together within a 2-week period along with either depressed mood or anhedonia. In addition to the PCL-C and PHQ-9, we also asked participants to report the year during which the Criterion A traumatic event was experienced and the age of onset of PTSD and depressive symptoms. These timing data were used to identify a study sample consisting only of participants who experienced their first major depressive disorder following a qualifying traumatic event.

The following variables were also included as possible confounds: gender (female vs. male), age, marital status (never married, divorced/separated/widowed, married), race (White, Black, other), annual income (≤ $60,000 vs. > $60,000), education (high school graduate, some college, college/graduate degree), insurance status (noninsured vs. insured), history of alcohol abuse based on *DSM-IV* criteria with onset prior to the PTSD-related traumatic event (yes vs. no), and deployment history (deployed vs. never deployed). Although men who have sex with men including those in the active and reserve forces are disproportionately affected by HIV (Levin et al., 1995), the survey did not assess same sex behavior and therefore we were unable to include this variable as a possible confounder.

Clinical interview. In addition to the CATI interviews and as part of the larger study, in-person clinical assessments were conducted on a random subsample of 500 participants. Master's- or doctoral-level clinicians fully consented the participants and conducted the clinical interviews. After consent was obtained, clinicians conducted the interviews in a location chosen by the participant. HIV risk behaviors were assessed using the same set of BRFSS questions listed in the telephone survey; however, in addition to the global measure of HIV risk (i.e., reporting one or more risk activities), participants completing the clinical interview were also asked to identify the specific set of behavior(s) in which they had engaged.

The Structured Clinical Interview for DSM-IV Disorders (SCID) was used to conduct detailed psychopathology assessments in the clinical subsample (First, Spitzer, Gibbon, & Williams, 2002). In the clinical reappraisal of the CATI assessments, we observed high specificity for PTSD (92%) and MDD (97%), and also found high internal consistency for PTSD (α = .93) and good internal consistency for MDD (α = .66; Calabrese et al., 2011). Clinical interviews typically lasted 2 hours and participants were compensated per hour for their time.

Data Analysis

As a first step, we compared the characteristics of persons reporting past-year HIV risk behavior with those reporting no risk behavior using chi-square tests or Fisher's exact test in the case of expected cell counts ≤ 5 in more than 20% of the cells. To examine the level of agreement between HIV risk behaviors reported during the CATI and those during the in-person interviews, we computed the kappa coefficient for responses from all participants who completed both types of assessments. To determine the independent and combined effects of PTSD and MDD, we then constructed an indicator variable consisting of four mutually exclusive categories: neither PTSD nor MDD, MDD only, PTSD only, and both PTSD and MDD. This variable was then included in a multivariable logistic regression model, adjusting for all other variables hypothesized *a priori* as possible confounders. All statistical analyses were conducted in SAS 9.2; all *p* values are two-sided.

Results

Sample Characteristics

The lifetime prevalence of PTSD in the sample was 7.9% (n = 178), and 145 persons (6.4%) screened positive for MDD. Past-year HIV risk behavior was reported by 142 participants (6.3%, 95%; CI = [5.3, 7.3]). As shown in Table 1, the subsample of participants with PTSD was more likely to report past-year HIV risk behavior, $\chi^2(1, N = 2,259) = 9.97$, $p = .002$, as were those with posttraumatic event MDD, $\chi^2(1, N = 2,259) = 7.78$, $p = .005$. Participants reporting HIV risk behavior were also more likely to be female, younger, single or of divorced/separated/widowed marital status, non-White, have

Table 1

Factors Associated With Reporting Past Year HIV Risk Behavior in Ohio Army National Guard Soldiers

Variable	HIV risk behavior (n = 142)		No HIV risk behavior (n = 2,117)		χ^2
	n	%	n	%	
PTSD					9.97**
No	121	85.2	1960	92.6	
Yes	21	14.8	157	7.4	
MDD					7.78**
No	125	88.0	1989	94.0	
Yes	17	12.0	128	6.0	
Sex					4.06*
Men	114	80.3	1828	86.3	
Women	28	19.7	289	13.7	
Age (years)					28.13***
17–24	69	48.6	638	30.1	
25–34	47	33.1	707	33.4	
35–44	22	15.5	548	25.9	
≥45	4	2.8	224	10.6	
Marital status					33.98***
Married	38	26.8	1086	51.3	
Divorced/separated/ widowed	15	10.5	197	9.3	
Never married	89	62.7	834	39.4	
Race					5.72
White	117	82.4	1874	88.5	
Black	17	12.0	145	6.9	
Other	8	5.6	98	4.6	
Income					9.61**
≤$60,000	100	70.4	1210	57.2	
>$60,000	42	29.6	907	42.8	
Education					2.24
High school graduate	41	28.9	561	26.5	
Some college	72	50.7	1001	47.3	
College/graduate degree	29	20.4	555	26.2	
History of alcohol abuse[a]					7.83**
No	134	94.4	2074	98.0	
Yes	8	5.6	43	2.0	
Insurance status					1.17
Insured	123	86.6	1895	89.5	
Noninsured	19	13.4	222	10.5	
Deployment history					2.23
Never deployed	54	38.0	677	32.0	
Deployed	88	62.0	1440	68.0	

Note. HIV = human immunodeficiency virus; PTSD = posttraumatic stress disorder; MDD = major depressive disorder.

[a]Only consider as *yes* those with onset prior to PTSD-related traumatic event.

*p < .05. **p < .01. ***p < .001.

lower annual income, and report a history of alcohol abuse (see Table 1).

Multivariate Analysis

The results of the multivariate logistic regression analysis are shown in Table 2. After adjustment for selected characteristics, screening positive for MDD (in the absence of PTSD) was found to be positively and independently associated with HIV risk behavior, adjusted odds ratio [*AOR*] = 2.3, 95% CI = [1.2, 4.7], compared to participants with neither condition. Posttraumatic stress disorder (in the absence of MDD) was not statistically significant, *AOR* = 1.6, 95% CI = [0.8, 3.2]. Finally, participants screening positive for both PTSD and MDD were most likely to report HIV risk behavior, *AOR* = 2.7, 95% CI = [1.1, 7.1].

Clinical sample characteristics. Among the subsample of 500 participants who completed the in-person clinical assessment, HIV risk behavior data was assessed and collected from 310. Of these participants, 24 (8.1%) reported engaging in at least one HIV risk behavior (95% CI = [5.1%, 11.1%]). In total, 16 (5.2%) reported unprotected anal intercourse, 9 (2.9%) reported being treated for a sexually transmitted disease, 4 (1.3%) had used intravenous drugs, and none reported exchanging sex for money or drugs in the past year. Of participants who completed both the CATI and in-person interviews, the level of agreement for reported HIV risk behavior was fair, κ = .58, 95% CI = [.41, .75].

Discussion

In this study of the Ohio Army National Guard, we observed a high prevalence of self-reported participation in HIV risk behavior. Screening positive for either PTSD or depression was found to be correlated with this outcome. Finally, soldiers reporting both PTSD and MDD after experiencing a traumatic event were most likely to report past-year HIV risk behavior.

The prevalence of HIV risk behavior observed in this study (6.4%) is higher than that found in a nationally representative sample of U.S. adults conducted in 2005, in which 4.0% reported past-year engagement in at least one of the HIV risk behaviors included in the BRFSS (Ohl & Perencevich, 2011). Interestingly, our results are comparable to the prevalence of BRFSS HIV risk behaviors found in other populations with adverse life experiences and exposure to trauma, including survivors of childhood abuse (7.6%), IPV (7.4%), and childhood cancer (8.3%; Bensley et al., 2000; Breiding, Black, & Ryan, 2008; Phillips-Salimi, Lommel, & Andrykowski, 2012). Given that over 90% of the OHARNG cohort has experienced at least one traumatic event (Calabrese et al., 2011), the comparable prevalence reported here to those observed in these studies is not entirely unexpected. It is also likely that the young and predominantly unmarried sociodemographic profile of the cohort,

Table 2

Multivariate Logistic Regression of Factors Associated With Reporting Past-Year HIV Risk Behavior

Variable	B	SE	AOR	95% CI	Wald χ^2
PTSD and MDD[a]					
PTSD only	0.47	0.35	1.60	[0.80, 3.20]	1.75
MDD only	0.85	0.36	2.33	[1.15, 4.71]	5.54*
PTSD and MDD	1.01	0.49	2.75	[1.06, 7.11]	4.32*
Sex[b]					
Women	0.09	0.24	1.10	[0.69, 1.74]	0.69
Age[c]					
25–34	-0.38	0.24	0.69	[0.43, 1.11]	2.40
35–44	-0.72	0.36	0.48	[0.25, 0.93]	4.68*
≥45	-1.52	0.57	0.22	[0.07, 0.67]	7.04***
Marital status[d]					
Divorced/ separated/widowed	0.77	0.33	2.16	[1.13, 4.10]	5.49*
Never married	0.79	0.25	2.20	[1.35, 3.57]	10.09***
Race[e]					
Black	0.60	0.29	1.82	[1.04, 3.18]	4.33*
Other	0.18	0.39	1.20	[0.56, 2.56]	0.21
Income[f]					
>$60,000	-0.03	0.21	0.97	[0.64, 1.47]	0.02
Education[g]					
Some college	0.06	0.21	1.06	[0.70, 1.61]	0.07
College/graduate degree	0.16	0.28	1.17	[0.68, 2.02]	0.31
History of alcohol abuse[h]					
Yes	0.84	0.51	2.31	[0.86, 6.22]	2.73
Insurance status[i]					
Noninsured	-0.14	0.27	0.87	[0.51, 1.47]	0.28
Deployment history[j]					
Deployed	0.10	0.21	1.11	[0.73, 1.67]	0.63

Note. $N = 2,259$. AOR = Adjusted odds ratio; CI = confidence interval; MDD = major depressive disorder; PTSD = posttraumatic stress disorder; HIV = human immunodeficiency virus.

[a]Neither MDD nor PTSD served as the reference group. [b]Men served as the reference group. [c]Ages 17–24 served as the reference group. [d] Married served as the reference group. [e]White served as the reference group. [f]Less than or equal to $60,000 served as the reference group. [g]High school graduate served as the reference group. [h]No served as the reference group. [i]Insured served as the reference group. [j]Never served as the reference group.

*$p < .05$. ***$p < .001$.

however, resulted in an HIV risk behavior prevalence greater than that observed in general population studies.

Our findings are also broadly consistent with an existing body of literature that has routinely demonstrated PTSD and depression to be positively associated with engagement in HIV risk behavior in nonmilitary populations (Alegría et al., 1994; Cavanaugh et al., 2010; Hutton et al., 2001; Perdue et al., 2003). Although there is a paucity of research examining the relationship between mental health problems and HIV risk in military

personnel, an analysis of data from the 1992 National Survey of Veterans showed that persons with comorbid PTSD and substance abuse disorders were at a greatly elevated risk of HIV infection (Hoff, Beam-Goulet, & Rosenheck, 1997). One recent study of soldiers in the Dominican Republic also found that PTSD was associated with sexual risk behavior (Tavarez et al., 2011). Although these aforementioned studies have demonstrated that PTSD is more strongly correlated with HIV risk behavior than depression (in contrast to our findings), neither examined the effect of comorbid mental health problems on HIV risk in a military population. Although further research is required, our results suggest that PTSD in the presence of other psychiatric conditions (e.g., depression) may have a greater influence on HIV risk behavior than PTSD on its own.

Although the cross-sectional nature of our work and these studies limit inference with respect to the causal relationship between PTSD, depression, and HIV risk, these findings suggest that interventions that aim to address psychiatric disorders among military personnel may have an ancillary benefit of reducing high-risk sex and drug-related behaviors. Irrespective of an underlying causal mechanism, our results indicate that soldiers suffering from both PTSD and depression should be the focus of future HIV prevention efforts. Although military-focused HIV prevention interventions have been implemented and are effective at reducing risk behavior in some settings (Bing et al., 2008; Ross et al., 2006; Russak, Ortiz, Galvan, & Bing, 2005), to our knowledge no studies have evaluated the efficacy of HIV prevention programs specifically for military personnel with mental illness. Given the significant burden of mental health problems in this population (Kehle et al., 2011; Milliken, Auchterlonie, & Hoge, 2007; Thomas et al., 2010), interventions that integrate psychiatric and HIV prevention services warrant development and evaluation.

A number of important study limitations must be noted. First, as the study instruments for the OHARNG Mental Health Initiative were not designed specifically to measure HIV risk, we were unable to conduct a thorough examination of behavioral risks for HIV acquisition in this population. For example, additional information regarding the context in which these behaviors take place (e.g., monogamous relationships or with casual partners of unknown serostatus) would have allowed for a deeper understanding of the true risks for HIV transmission experienced by soldiers of the OHARNG. Second, the cross-sectional nature of our analysis precludes a causal interpretation of the observed associations. Third, we were not able to examine more antecedent components of the hypothesized etiologic pathway, including the potentially direct relationship between exposure to trauma and HIV risk behavior in the absence of PTSD. Fourth, a small number of participants were unable to recall the precise timing of these conditions and were excluded. Fifth, our measure of HIV risk was self-reported, and thus may be susceptible to underreporting, particularly given the stigmatized nature of the assessed behaviors. Although the higher prevalence of HIV risk behavior observed among participants completing the in-person clinical assessment does suggest some

underreporting in the larger CATI sample, the relatively small difference of these values (i.e., 8.1% vs. 6.4%) indicates that the magnitude of potential bias from underreporting is minimal. We cannot, however, exclude the possibility that HIV risk was underreported in both the CATI and clinical interviews. Sixth, the observed relationships between depression, PTSD, and HIV risk may be due to residual or unmeasured confounding. Finally, although our results are strictly generalizable to soldiers willing to participate in the research, we note that the characteristics of our sample are similar to those of the OHARNG (Calabrese et al., 2011), and are thus likely representative of the larger population.

In summary, this study demonstrated that mental health problems, notably PTSD and depression, were prevalent and associated with increased engagement in HIV risk behaviors among a sample of Ohio Army National Guard. These findings suggest that mental health problems including depression and PTSD play a role in augmenting vulnerability to HIV in this population. Given the expanding role of National Guard in combat operations and the commensurate increase in exposure to traumatic events, effective interventions are required to support soldiers at risk for HIV and prevent future infections.

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Preliminary communication

Cigarette smoking and subsequent risk of suicidal ideation among National Guard Soldiers

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ABSTRACT

Background: Suicide rates are alarmingly high among military personnel, and particularly Army National Guard soldiers. Smoking is also disproportionately common in the military. In this study, we intend to investigate the relationship between cigarette smoking and suicidal ideation among a representative sample of national guard soldiers.
Methods: A representative sample of Ohio Army National Guard soldiers were followed prospectively and information was gathered on smoking, suicidal ideation and depression at baseline and one year later.
Results: Smoking at baseline was associated with significantly increased likelihood of suicidal ideation at follow-up (OR=2.0 (1.3, 3.2)). This association persisted after adjusting for demographics and history of depression at baseline, but was no longer statistically significant after adjusting for depression at follow-up.
Limitations: Measurement of smoking was somewhat limited.
Conclusions: Army National Guard soldiers who smoke have a greater risk of subsequent suicidal ideation. Depression concurrent with suicidal ideation appears to explain this relationship. If these results are replicated, screening of soldiers who smoke may be recommended as a proactive step towards mitigating the high risk of suicide in military personnel.

1. Introduction

Military populations are at high risk for suicidal behavior and suicide rates in the military continue to rise (Kuehn, 2009). Suicide rates in the US military have increased in recent years, and the most dramatic increase has been among Army National Guard members (Griffith, 2012). Suicide rates in the Army National Guard are now higher than rates among active duty army personnel (U.S Army Office of the Chief of Public Affairs, 2010).

Smoking is also disproportionately prevalent among soldiers (Smith and Malone, 2009). Cigarettes were included as part of meal rations during World War I and II and the Vietnam War (2010). It was not until the early 1970s that the United States (US) Department of Defense issued policies aimed at preventing and

treating substance abuse; by 1975 cigarettes were no longer rationed to soldiers (Ames et al., 2007). Trend data show that over the past 28 years cigarette smoking in the US military has decreased; however, the prevalence of cigarette smoking has remained higher among military personnel compared to the general population: approximately 32% of active duty military personnel are smokers compared to 21% of US adults (Bray and Hourani, 2007).

Results from numerous epidemiologic studies have consistently documented a strong association between cigarette smoking and suicide-related outcomes among adults in the community (Breslau et al., 2005; Kessler et al., 2007; Kessler et al., 2009). Only one study has examined this relationship among military personnel. Miller et al. (2000) found that smoking was associated with completed suicide among active duty male army soldiers. The study did not consider key potentially mediating factors, such as depression.

Since that study, several things have changed. Active military conflicts over the past decade have led to increased military personnel; each year the US military brings in 300,000 new

recruits. Since the start of Operation Iraqi Freedom and Operation Enduring Freedom, National Guard members have been called upon increasingly to serve in combat situations. As of January 2010, there were over 1.1 million active duty personnel serving in the four branches of the US military and 131,066 personnel serving in the National Guard. National Guard members are a distinct and sizable subset of the military, increasingly relied upon for active duty deployments. However, compared with active/full-time military, relatively little is known about mental health risks in this group. In addition, National Guard members are outside the support structures provided to regular military personnel and are, therefore, exposed to an especially heavy burden of chronic civilian stressors post-deployment (e.g., family conflict, job loss) without the benefit of adequate resources to cope with such stressors. Finally, as noted above, the rate of suicide among National Guard members has increased substantially in the past few years (Griffith, 2012).

To our knowledge, no previous study has examined the potential impact of smoking on subsequent suicide-related outcomes in a reservist population. The current study examined the relationship between smoking and subsequent risk of suicidal ideation in 2010 in a representative sample of Army National Guard soldiers.

2. Methods

2.1. Study population and survey

Data were drawn from the Ohio Army National Guard Mental Health Initiative (OHARNG MHI). The OHARNG MHI is a longitudinal cohort of Ohio Army National Guard Soldiers who are interviewed annually to assess mental health, substance use and life experiences. All soldiers were asked to participate in the study with the option to opt out. Of the soldiers enlisted between June 2008 and Feb 2009, 11,212 soldiers did not opt out of the study, and accurate contact information was available for 58.1% of participants ($n=6,514$). This group was further reduced to a final baseline sample of 2,616 after eligibility, language proficiency, and desire to participate were taken into account; survey response rate was 43.2%. Participants were contacted for follow-up interviews in November of 2009, within 12 months of their original interview, and given 12 months to respond. 67.7% of the original 2,616 soldiers responded to follow-up surveys ($n=1,770$). This study included the 1,770 soldiers who participated in both baseline and follow-up surveys. After giving written informed consent, soldiers participated in computer-assisted telephone interviews that obtained information on mental health, substance use, military experiences, and life events history. The investigation was carried out in accordance with the latest version of the Declaration of Helsinki. The study design was reviewed by University of Michigan and Case Western IRB and informed consent of the participants was obtained after the nature of the procedures had been fully explained.

Our main dependent variable of interest was whether or not an individual reported having suicidal thoughts, or thoughts of being better off dead or wanting to hurt themselves, at some point between the baseline survey and the follow-up survey. Suicidal ideation was assessed via the question from the Patient Health Questionnaire-9 (PHQ-9) which asked if individuals ever thought of harming themselves or that they would be better off dead (Kroenke et al., 2001).

Our main independent variable of interest was whether or not individuals reported that they smoked within 30 day of the baseline survey. Smoking status was also recorded at follow-up

assessing if participants reported smoking at any point between their baseline and follow-up survey.

Other covariates included presence of suicidal behavior at baseline and depression at baseline, smoking status at follow-up and depression at follow-up, and age and gender. Depression was assessed using the Patient Health Questionnaire-9 (Kroenke et al., 2001). To have had a history of depression at baseline, individuals had to have at least 2 co-occurring symptoms at some point in the past (Kroenke et al., 2001). To have depression at follow-up, the individual had to have had the same number of symptoms but they must have occurred between the baseline survey and follow-up survey. A concurrent clinical reappraisal conducted with the OHARNG MHI found the PHQ to be highly specific, when compared to clinician-administered interviews (Calabrese et al., 2011). The presence of the conditions (Yes vs. No), gender (female vs. male) and age were included as indicator variables (18–24 (reference), 25–34, 35–44, 45+).

2.2. Statistical analysis

First, for everyone who completed a baseline and follow-up survey, and completed questions on smoking at follow-up ($N=1766$), we compared the distribution of suicidal ideation at follow-up according to baseline and follow-up characteristics using bivariable logistic regression. Second, we used multivariable logistic regression to estimate the relation between smoking status at baseline, and suicidal ideation at follow-up. We ran three multivariable models: (a) we adjusted for potential confounders including age and gender, (b) we adjusted for possible confounders of the effect of baseline smoking on subsequent suicidal ideation including age, gender, depression at baseline and suicidal thoughts at baseline, and (c) to isolate the effect of smoking on subsequent suicidal ideation, we used logistic regression adjusting for age, gender, suicidal ideation at baseline, depression at baseline, smoking status as follow-up and depression at follow-up. Finally, we performed sensitivity analysis using the PHQ-8, omitting the suicidal ideation question from the PHQ-9. All analyses were carried out using SAS 9.2.

3. Results

The distribution (number (%)) and the association (crude odds ratio, 95% CI) of suicidal ideation at follow-up by baseline and follow-up characteristics is shown in Table 1. 30.5% of the sample reported smoking at baseline, the majority of the sample was male (86.1%) and below the age of 35 (64.3%). At baseline, 21.2% of soldiers had a lifetime history of depression and 10.2% had a history of suicidal ideation. At follow-up, 29.6% of soldiers smoked, 12.3% had depression in the past year, and 4.2% reported suicidal ideation in the past year. In bivariable associations, smoking status at baseline was associated with suicidal ideation and answered all follow-up questions ($N=1766$) at follow-up (crude odds ratio COR=2.0, 95% confidence interval CI: 1.3–3.2). In addition, history of depression at baseline (COR=5.1, 95% CI: 3.2–8.2), suicidal ideation at baseline (COR=8.0, 95% CI: 4.9–13.0), smoking status at follow-up (COR=2.2, 95% CI 1.4–3.6), and depression at follow-up (COR=19.2, 95% CI: 11.5–32.1) were all associated with suicidal ideation at follow-up.

The adjusted associations (adjusted odds ratio AOR, 95% CI) for the effect of smoking status at baseline and subsequent suicidal ideation are presented in Table 2. Adjusting for age and gender, those who smoked at baseline were more likely to have suicidal thoughts at follow-up (AOR=2.0, 95% CI: 1.3–3.2). However, this effect was not robust and was minimal once we controlled for

Table 1
Distribution of selected characteristics in the total sample and association of suicidal thoughts in the follow-up survey.

Characteristics	Total sample (number (%))	Those with suicidal ideation at follow-up (number (%))	COR (95% CI)
Smoked at baseline			
No	1228 (69.5)	40 (3.3)	1
Yes	538 (30.5)	34 (6.3)	2.01 (1.26–3.21)
Gender			
Male	1520 (86.1)	59 (3.9)	1
Female	246 (13.9)	15 (6.1)	1.6 (0.90–2.88)
Age			
18–24	552 (31.3)	26 (4.7)	1
25–34	582 (33.0)	22 (3.8)	0.80 (0.45–143)
35–44	438 (24.8)	17 (3.9)	0.82 (0.44–2.53)
45+	193 (10.9)	9 (4.7)	0.99 (0.46–2.15)
History of depression at baseline			
No	1391 (78.8)	33 (2.4)	1
Yes	375 (21.2)	41 (10.9)	5.08 (3.16–8.16)
History of suicidal thoughts at baseline			
No	1583 (89.6)	42 (2.7)	1
Yes	180 (10.2)	32 (17.8)	7.98 (4.89–13.0)
Smoked at follow-up			
No	1244 (70.4)	39 (3.1)	1
Yes	522 (29.6)	35 (6.7)	2.23 (1.40–3.56)
Depression at follow-up			
No	1549 (87.7)	24 (1.6)	1
Yes	217 (12.3)	50 (23.0)	19.2 (11.5–32.1)
Total	**1766**	**74 (4.2)**	

Table 2
Adjusted association between the covariates of interest and suicidal ideation after one year of follow-up.

	AOR (95% CI)	AOR (95% CI)	AOR (95% CI)
Smoked at baseline			
No	1	1	1
Yes	2.01 (1.25–3.22)	1.69 (1.03–2.77)	1.12 (0.46–2.70)
Gender			
Male	1	1	1
Female	1.58 (0.88–2.87)	1.32 (0.71–2.45)	1.17 (0.60–2.29)
Age			
18–24	1	1	1
25–34	0.84 (0.47–1.51)	0.80 (0.43–1.46)	0.67 (0.34–1.30)
35–44	0.95 (0.50–1.79)	0.95 (0.49–1.85)	0.89 (0.44–1.81)
45+	1.16 (0.53–2.54)	1.04 (0.46–2.36)	1.07 (0.45–2.53)
History of depression			
No		1	1
Yes		2.74 (1.58–4.73)	1.37 (0.77–2.45)
History of suicidal thoughts			
No		1	1
Yes		4.64 (2.65–8.12)	4.17 (2.32–7.50)
Smoked at follow-up			
No			1
Yes			1.57 (0.65–3.79)
Depression at follow-up			
No			1
Yes			13.2 (7.59–23.0)
−2 Log likelihood	**603.0**	**535.5**	**445.2**

depression (AOR=1.1, 95% CI: 0.5–2.7) and smoking at follow-up. Sensitivity analysis excluding suicidal ideation as a symptom of depression did not show any differences from these findings (data not shown).

4. Discussion

The prevalence of suicide in Army National Guard members has been increasing since 2006 and in 2010 exceeded the rate

among active duty army personnel (Griffith, 2012). Suicidal ideation is a significant predictor of future suicide behavior, but is also associated with substantial impairment and distress even when it does not lead to suicide behavior (Olfson et al., 1996). To our knowledge, this is the first study to examine the relationship between smoking and subsequent suicidal ideation in a National Guard population. Our results suggest that active smoking is associated with increased suicidal ideation at follow-up among National Guard soldiers.

There are a number of plausible explanations for this association. One possibility is that smoking leads to increased depression that then increases the risk of suicidal ideation. There is a well-documented relationship between cigarette smoking and increased levels of inflammation (Garbin et al., 2009) A relationship between major depression and inflammation is also well-documented (Glover et al., 2009; Halder et al., 2010; Miller, 2010; Miller et al., 2009; Pace and Miller, 2009; Su et al., 2009). It is thought that the release of specific inflammatory markers and activation of the immune system may be related to the pathophysiology of depression potentially via the effects of cytokines on specific regions of the brain (Pace and Miller, 2009). Major depression is the strongest known risk factor for suicide behavior (Fawcett et al., 1987), and suicide ideation is so entwined with depression that it is part of the diagnostic criteria for major depression (American Psychiatric Association, 1994). As such, it is reasonable to postulate that inflammation may be related to suicide behavior through similar pathways. Our data support this pathway (i.e., that depression is a mediator of the relationship). It is also conceivable that the relationship is due to other common causes that we could not evaluate in this study. While it is not possible to definitively identify the mechanism in this study and some studies have suggested that the association between smoking and suicide-related outcomes may be due to confounding (Hemmingsson and Kriebel, 2003; Smith et al., 1992), the potential importance of smoking as a screen in evaluating suicide risk in this high risk group is clearly supported by our findings.

This study has several limitations that should be considered when interpreting our results. First, we did not have measures of suicide attempt or completion. Suicidal ideation is highly correlated with these behaviors (Beck et al., 1999; Brown et al., 2000; Kessler et al., 2009; Mann et al., 1999), and one study of male active-duty army soldiers found a link between smoking and suicide though this study did not adjust for depression (Miller et al., 2000). Future studies that can take depression and other mental disorders into account while examining the relationship between smoking and other suicide-related outcomes over time in various military populations are needed. Second, although there is no reason to believe that Ohio Army National Guard members are systematically different from other reservists nationwide, it is possible that our findings may not be generalizable to other National Guard and/or active military personnel. Therefore, additional studies in these vulnerable populations should be carried out toward replicating these results. Third, our ability to test potential mechanisms of the relationship between smoking and suicidal ideation was limited. Future studies in military samples will be needed to examine potential mechanisms of these relationships.

If these findings are replicated, future screening efforts that include an assessment of active smoking behavior may suggest National Guard members at greater risk of suicidal ideation, and potential suicidality.

Conflict of interest

The authors report no conflicts of interest.

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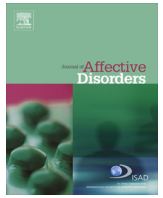
Research report

Validation of the telephone-administered PHQ-9 against the in-person administered SCID-I major depression module

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ABSTRACT

Background: We assessed item-to-item correspondence between the Patient Health Questionnaire-9 (PHQ-9) and the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) major depression episode portion of the major depressive module.
Method: Four hundred and ninety-eight soldiers in the Ohio National Guard were administered the PHQ-9 and SCID-I. Data were analyzed using chi-square analyses, logistic regression, receiver operating characteristic (ROC) curve analyses and diagnostic efficiency statistics.
Results: To screen for depression effectively, results indicate use of the cardinal first two items, items representing fatigue, appetite and sleep changes with an item level cut-off point of two, and the item representing suicidal ideation with item level cut-off point of one. Further, total PHQ-9 scores significantly predicted SCID-I major depressive episode (MDE) and diagnosis (MDD) with moderate accuracy. Lastly, the cut-off total score of 10 had the optimal balance of sensitivity and specificity compared to other PHQ-9 scoring options.
Limitations: Differences in timeline of administration of the measures, differences in "worst episode" reference between the measures, and use of a specific military population are some of the limitations.
Conclusions: This validation study provides guidelines for the use of the telephone-administered PHQ-9 in assessing the lifetime prevalence of a major depressive episode and diagnosis in non-clinical populations, with implications for clinical use.

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1. Introduction

Valid screening instruments are important to accurately assess depression in large-scale population-based research. However, there is limited research validating the use of screening instruments against clinical re-interviews with assessments considered the "gold standard." The Patient Health Questionnaire-9 (PHQ-9), developed as an self-report depression screen for primary care, has shown to accurately detect lifetime major depressive disorder using the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) major depression module as the "gold standard" (Cannon et al.,

2007). However, little is known about the validity of a telephone-administered PHQ-9 in detecting lifetime depression diagnosis.

Telephone administered assessments play an important role in public health research and practice (Kempf and Remington, 2007). Advantages of this approach include geographical accessibility (Pinto-Meza et al., 2005), efficiency with the temporal nature of variables (Kempf and Remington, 2007), flexibility and reduced financial costs (Bonnel and Le Nir, 1998; Kempf and Remington, 2007; Pinto-Meza et al., 2005). Some concerns about telephone administered assessments include difficulty understanding complex wording of questions, problems in remembering questions, and inability to better assess the respondent's understanding and attention span (Bonnel and Le Nir, 1998). Further, there is unresolved debate about whether sensitive information is reported on the telephone (De Vries et al., 2005; Kempf and Remington, 2007). Several studies have successfully validated telephone interviews against in-person administrations of the same instrument

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to assess depression; reported instruments include the Structured Clinical Interview for DSM-III-R (SCID-I), Hamilton Depression Rating Scale (Simon et al., 1993), the Spanish version of the Geriatric Depression Scale (Carrete et al., 2001), and the Center for Epidemiologic Studies-Depression Scale (Aneshensel et al., 1982). Relevant to the current study are findings indicating that the telephone administration of the PHQ-9 has comparable internal consistency, good agreement, and adequate procedural validity compared to its in-person administration within a 7-day period (Pinto-Meza et al., 2005).

The PHQ-9, a 9-item module from the Primary Care Evaluation of Mental Disorders assessment (PRIME-MD) (Spitzer et al., 1994) is widely used as a measure of depression severity (Kroenke et al., 2001). Advantages of the PHQ-9 include brevity, strong psychometric properties, and the ability to reflect subjective experiences of depression (Malpass et al., 2010), detect changes in depression severity over time (Löwe et al., 2003; Malpass et al., 2010), and measure depression outcomes, comparable to the SCID (Löwe et al., 2003). However, several weaknesses of the PHQ-9 have been suggested, including inaccuracy in assessing the presence, experience and intensity of self-harm thoughts and inadequate coverage of all aspects of depression (Malpass et al., 2010).

Several studies have validated the self-report administration of the PHQ-9 using the SCID-I, a semi-structured interview for assessing DSM-IV Axis I disorders (First et al., 1997). There has been support for the validity of the self-report administered PHQ-9 with a clinician administered SCID-I diagnoses of major depressive episode's criterion A, satisfying the symptom criteria but no requirements regarding functional impairment or ruling out other conditions (Cannon et al., 2007). Further, Cannon et al. (2007) validated the self-report administered PHQ-9 in relation to lifetime major depressive episode (MDE) and major depressive disorder (MDD) as assessed by the SCID. Further, the self- report administered PHQ-9 better serves as a screening instrument using a cut-off point of 10 or greater (sensitivity of .93 and a specificity of .85) rather than a diagnostic tool using the diagnostic algorithm (sensitivity was .68 and specificity was .95), when validated with the SCID depressive disorder module (Wittkampf et al., 2009). No study, as far as we are aware, has validated the telephone-administered PHQ-9 against an in-person administered SCID-I depression module, which is the focus of the current study.

There is an additional question about the optimal PHQ-9 cut-off scores to maximize sensitivity (proportion of people who meet the criteria as per the PHQ-9 using the gold standard) and specificity (proportion of people accurately detected as not meeting a certain criteria by the PHQ-9 using the gold standard) in detecting a depression diagnosis. Some studies support "10" as a cut-off score, with sensitivity ranging from 74 to 88% and specificity ranging from 88 to 91% (Arroll et al., 2010; Kroenke et al., 2001). However, other studies have suggested different cut-off points, including a cut-off score of 6 or higher in a sample of adult women (Hanusa et al., 2008). Another option suggested was to use either "2" or "3" as the cut-off score at the item level ratings, depending on desired sensitivity and specificity (Cannon et al., 2007). Results indicated that lowering the minimum required positive response value from 3 to 2 raised sensitivity from 53% to 69% but lowered specificity from 93% to 86%, which was not completely consistent with the findings of Kroenke et al. (2001), Cannon et al. (2007).

Kroenke et al. (2001) described a diagnostic algorithm for using the PHQ-9: probable major depressive disorder is considered if at least five out of the 9 symptoms are endorsed at least "more than half the days," (rating of two) and "other depression" is diagnosed if one endorses two, three, or four depressive symptoms at least "more than half the days." For both depression diagnostic judgments, the timeline is the past two weeks and one of the symptoms has to be depressed mood or anhedonia per DSM-IV criteria (Kroenke et al., 2001). A meta-analysis (Wittkampf et al., 2007) compared the diagnostic algorithm

with a cut-off score of 10 or higher in several studies. With the algorithm, specificity was 94% and sensitivity was 77%. However, with the cut-off score of 10 or higher, the sensitivity and specificity were both 88%. Based on this analysis, using cut-off scores rather than the diagnostic algorithms may be preferable (Wittkampf et al., 2007). Another study validating the self-report administered PHQ-9 against the SCID-I depression module in a geriatric sample found that in contrast to using a cut-off score of 10, a cutoff of 9 or greater increased sensitivity from 63% to 88%, while sensitivity only slightly decreased from 82% to 80% (Phelan et al., 2010). Using the data from the current sample, Prescott et al. (In Press) have completed a validation of the key mental health assessments in the telephone survey which include the PHQ-9 using the Kroenke diagnostic algorithm for scoring. We have performed a more detailed comparison of the PHQ-9 and the SCID using both item-by-item analysis and multiple cut points.

The current study contributes to the existing literature in several ways. We know of no study that has validated a telephone administration of the PHQ-9 against an in-person administered SCID-I depression module as the "gold standard," with an item-to-item relational analyses. Specifically, we evaluate the use of the PHQ-9 cardinal items to screen depression. We also report the relationship of the final seven items of the PHQ-9 with the corresponding SCID-I items. There is ongoing debate about the optimal cut-off score for the PHQ-9, and whether to use the diagnostic algorithm or a cut-off score, with implications for under-diagnosis and over-diagnosis of depression (Wittkampf et al., 2007). We evaluate the ability of total PHQ-9 scores to predict the minimum depressive symptoms needed for an MDE (MDE Criterion A), a MDE and a MDD per the SCID-I. We also examine diagnostic efficiency statistics comparing the diagnostic algorithm to the cut off scores of 10, 15 and 20.

This study uses an epidemiological sample of National Guard Soldiers, which is rare in the existing literature validating depression instruments. Most of the studies using the PHQ-9 have used samples with medical or psychological needs, including primary care patients (Arroll et al., 2010; Kroenke et al., 2001; Malpass et al., 2010; Phelan et al., 2010; Wittkampf et al., 2009); outpatient medical care patients (Fann et al., 2009; Löwe et al., 2003; Turvey et al., 2007); samples with mental health needs (Eack et al., 2006); and community samples (Cannon et al., 2007). Lastly, there is dearth of research with reference to the question of the use of the PHQ-9 for diagnosis of MDE Criterion A, MDE or MDD; this issue is relevant to the diagnostic validity of the PHQ-9.

2. Method

2.1. Participants and procedure

The current study analyzed data collected as part of the Ohio Army National Guard (OHARNG) Mental Health Initiative, which assessed various aspects of mental health among Ohio National Guard soldiers. The primary aim of this project was to assess for mental health risk and resiliency factors longitudinally among military veterans. The study involved a computer assisted telephone interview (CATI) conducted by trained lay interviewers. A subsample of 500 participants was randomly chosen for in person clinical reappraisals conducted by trained clinician interviewers.

The initial population comprised all members of the Ohio National Guard serving between July 2008 and February 2009. Among the 12,225 Guard members with a valid mailing address, potential subjects were excluded for not having correct or working phone numbers ($n=3568$), not having a number listed with the Guard ($n=1130$) and declining to participate in the study (opting out of the study when receiving the original participation letter)

($n=1013$), leaving a sample of 6514 Guard members (58.1%). Additionally, other exclusion criteria in this reduced pool were age eligibility restrictions ($n=187$), declining to participate when contacted by phone ($n=1364$), having English language or hearing difficulties ($n=31$), and not being contacted before the cohort was closed to new recruitment ($n=2316$). Thus, the final sample comprised 2616 soldiers drawn from all of the serving members of the OHARNG, who were given their baseline computer-assisted telephone interview starting in November 2008. Enrollment for the study continued from December 2008 to November 2009. The study received approval from the National Guard Bureau, Office of Human Research Protections of the U.S. Army Medical Research and Materiel Command, and affiliated hospital and university institutional review boards. Further, verbal consent on the telephone was permitted via a waiver of written informed consent.

A clinical validation sub-sample ($n=500$) was randomly chosen during the baseline telephone survey and upon providing written consent was subsequently given an in-person interview, which was the sample used in the current study. Of the 500 subjects, two subjects were excluded from the analyses because they endorsed a new onset of depression during SCID administration (i.e., after the PHQ-9 administration). Further, 10 subjects missing 1–2 PHQ-9 items were not excluded from the study, resulting in a final sample size of 498 soldiers.

2.2. Instrumentation

The CATI and in-person clinical reappraisal obtained demographic information, and information on mental health functioning using several standardized and widely used questionnaires (Prescott et al., In Press). The PHQ-9 administered by telephone and the SCID-I administered in-person are relevant to the current study.

2.2.1. Patient Health Questionnaire-9 (PHQ-9)

The PHQ-9 is a Likert-type self-report instrument assessing symptoms of current depression based on DSM-IV major depressive episode symptom criteria. For each item there were four response options ranging from "0=*Not at all*" to "3=*Nearly every day*" with total scores ranging from zero to 27. The cut-off scores of 5, 10, 15 and 20 represent mild, moderate, moderately severe, and severe depression, respectively. The scoring algorithm for major depression is consistent with DSM-IV diagnostic criteria, with 5 out of 9 statements endorsed minimally as "more than half the days," and one of the symptoms being depressed mood or anhedonia. Internal consistency ranges from .86 to .89 (alpha was .84 in the present study), and test–retest reliability within 48 h is 0.84. The PHQ-9 has good diagnostic validity for an MDD diagnosis based on structured diagnostic interviews. Good correspondence between PHQ-9 severity scores and measures of functional status, number of disability days and difficulties based on symptoms indicate good construct validity (Kroenke et al., 2001). Given that the original instructions of the PHQ-9 focus on distressing symptoms of the past two weeks consistent with the DSM-IV criteria, the current study modified the instructions to assess lifetime depression. Instructions used in the current study during the telephone administration were: "In your lifetime, did you ever have a period of at least two weeks during which you were bothered by (item)."

2.2.2. Structured Clinical Interview for DSM-IV axis I disorders (SCID-I)

The SCID-I is a semi-structured interview for assessing DSM-IV Axis I disorders, including major depressive disorder (First et al., 1997). The major depressive disorder module has an inter-rater reliability coefficient ranging from .66 to .93 (Lobbestael et al., 2010; Zanarini and Frankenburg, 2001). For the current study, the SCID was administered by PhD or Masters level clinician interviewers specifically trained on the SCID. To reduce inter-rater differences, a taped interview was reviewed and rescored by the non-interviewing clinicians monthly. The scores were compared for differences, and discussed among interviewers to continually re-calibrate SCID item assessment. Overall, the SCID-I is considered to be the "gold standard" used in validation studies for Axis I clinical disorders (Lobbestael et al., 2010).

Additionally, the current study used three categorizations of the SCID-I lifetime depression designations: (1) the minimum five-symptom requirement for a major depressive episode (with at least anhedonia and/or depressed mood being met), regardless of rule-out criteria and functional impairment requirements (MDE Criterion A), (2) full MDE criteria, thus including rule-out and functional impairment requirements, and (3) an MDD diagnosis, thus including additional diagnostic rule-outs. Further, the SCID-I provided data on lifetime endorsement of depression symptoms, as the queries for information pertained to current and lifetime symptoms.

2.3. Statistical analysis

Chi-square analyses were used to analyze the item-level correspondence between the PHQ-9 and SCID-I. Further, logistic regression analyses aimed to study the predictive relationship between the PHQ-9 and SCID-I cardinal first two items, and the predictive relationship between total PHQ-9 scores and designation of depression based on the SCID-I depression diagnosis (minimum number of depression symptoms needed for a major depressive episode, MDE, and MDD). Lastly, receiver operating characteristic curve analyses, and diagnostic efficiency statistics of sensitivity, and specificity aimed to assess the optimal cut-off point for the PHQ-9 (Streiner, 2003; Streiner and Cairney, 2007). All statistical analyses were computed using SPSS 17 software.

3. Results

3.1. Effective sample characteristics

In the effective sample of 498 participants, age ranged from 17 to 60 years ($M=31.04$, $SD=9.81$). The majority were men ($n=438$, 88%), and there were 60 women (12%), which is representative of the Ohio Army National Guard population. Further, 47.8% participants were currently married ($n=238$), and 41.8% had never been married ($n=208$). Most participants identified their race as Caucasian ($n=443$, 89.1%), with 6.8% identifying their race as African American ($n=34$), again representative of the Ohio Army National Guard population. Very few participants were of Hispanic ethnicity ($n=12$, 2.4%). The most frequently endorsed educational category was that of college or technical training education ($n=238$, 47.8%), followed by that of a high school degree or GED ($n=128$, 25.7), and a college degree ($n=123$, 24.7%). Further, most were primarily employed full-time ($n=287$, 57.9%), followed by 13.5% being employed part-time ($n=67$), 17.1% being unemployed ($n=85$), and 9.9% being students ($n=49$, 9.9%). Additionally, 71 participants reported household income of $20 K or less (14.6%), 110 reported more than $20 K and up to $40 K (22.6%), 113 reported more than $40 K to $60 K (23.2%), 87 reported more than $60 K to $80 K (17.9%), and 106 reported more than $80 K (21.8%). Number of years of military service ranged from zero to 40 years ($M=10.22$, $SD=8.62$). Further, the number of deployments among participants varied. Some had never been deployed ($n=172$, 34.7%), or were deployed once ($n=149$, 30%), twice

($n=101$, 20.4%), or three times ($n=42$, 8.5%). Among those deployed, 42.4% ($n=137$) had been deployed to Iraq, 26.9% ($n=87$) to Kuwait and Saudi Arabia ($n=87$, 26.9%) and 16.7% ($n=54$) to the United States.

Among the 498 subjects, 289 were not administered the full SCID-I depression module because of skip-out rules required for non-symptomatic responding. Two-hundred and nine subjects endorsed either (or both) of the sadness and anhedonia items, thus were administered the remaining SCID-I depression symptom items, used in analyses involving the remaining SCID-I depression items. Demographic data for those 209 subjects (administered the entire SCID-1 depression module) were compared with that of the remaining 289 subjects (not administered the entire SCID-I depression module) using ANOVA for continuous variables such as age, number of years in the military and number of deployments, and chi-square analyses for categorical variables. Results of ANOVAs indicated that the two subsamples did not differ significantly at $p < .05$ in participants' age, number of years in the military, and number of deployments. Results of chi-square analyses are shown in Table 1, indicating a significant association between endorsing either (or both) of the sadness and anhedonia items and income, $\chi^2(4)=14.04$, $p=.007$, $phi=0.17$.

3.2. Primary analyses

The percentage of lifetime MDE and lifetime MDD based on the SCID-I diagnostic module were 24.3 and 21.5, respectively. Further, the percentage of lifetime MDE based on the PHQ-9 scoring algorithm, cut off scores of 10 or more, 15 or more, and 20 or more was 13.10%, 25.10%, 11.80%, and 3.20%, respectively.

The results of the analysis of the relationship between (a) the PHQ-9′s depression item (item 2), and SCID-I's depressed mood item (item 1), and (b) between the PHQ-9′s anhedonia item (item 1) and SCID-I's anhedonia item (item 2) using chi-square analyses and logistic regression are presented in Table 2. With PHQ-9 items dichotomized using "2" as the cut-off score for positive endorsement, chi-square analyses indicated a significant association between the PHQ-9 and SCID-I on the depressed mood item, $\chi^2(1)=83.57$, $p < .001$ and anhedonia item, $\chi^2(1)=28.36$, $p < .001$, with the degree of agreement represented by their respective Kappa values as fair. The odds of endorsing the PHQ-9 depressed mood item were 7.58 times greater if the subject endorsed the SCID-I depression item; while odds of endorsing the PHQ-9 anhedonia item were 3 times greater if the subject endorsed the SCID-I anhedonia item.

Further, logistic regression was computed to assess the predictive relationship of the first two PHQ-9 items' range of scores with SCID-I item endorsements for the relevant two items (anhedonia and depressed mood). For the depressed mood item, results indicated that the model tested with PHQ-9 depression item scores as the predictor was statistically significant, $\chi^2(1)=107.77$, $p < .001$ (Nagelkerke's $R^2=.27$). The proportion of cases accurately predicted was 73.80%. Each increase of 1 unit in the PHQ-9 item was associated with a 2.46 times greater likelihood of endorsing the relevant SCID-I item. For the anhedonia item, results indicated that the model tested with PHQ-9

Table 1
Results of chi-square analyses comparing demographic variables between the group positive for at least one cardinal depression symptom and the group negative for any cardinal symptom.

Categorical variable compared to the category of endorsing either (or both) of the sadness and anhedonia items	χ^2	Degrees of freedom (df)	Significance value (p)
Marital status (married currently or in the past and never been married)	1.34	1	0.25
Educational status (high school/GED or less, some college and college degree/graduate work)	1.94	2	0.38
Employment status (employed full-time or part-time, unemployed or looking for work, and unemployed)	0.52	2	0.10
Income ($< =20,000$, \$20,001–\$40,000, \$40,001–\$60,000, \$60,001–\$80,000, $> 80,000$)	14.04	4	0.007*
Self-reported ethnicity (Caucasian and others).	0.31	1	0.58
Location of deployment (USA/Afghanistan, Iraq, Kuwait and Saudi Arabia)	2.01	2	0.37
Gender (male and female)	3.62	1	0.057

* Significant at $p < .05$.

Table 2
Chi-Square values with significance levels, kappa coefficients and sample sizes for each of the seven PHQ-9.

PHQ-9 item with corresponding SCID-I item	Sample size	Chi-square values	Significance level	Kappa coefficients
Depressed Mood (PHQ-9 item 2, dichotomized and SCID-I item 1) *Item level cut-off point of 2*	480	$\chi^2(1)=83.57$	**$p < .001$	.40
Anhedonia (PHQ-9 item 1, dichotomized and SCID-I item 2) *Item level cut-off point of 2*	479	$\chi^2(1)=28.36$	**$p < .001$	.24
Appetite (PHQ-9 item 5, dichotomized and SCID-I item 3) *Item level cut-off point of 2*	209	$\chi^2(1)=4.79$	*$p=.03$	.14
Sleep (PHQ-9 item 3, dichotomized SCID-I item 4) *Item level cut-off point of 2*	209	$\chi^2(1)=4.84$	*$p=.03$	.14
Motor activity (PHQ-9 item 8, dichotomized and SCID-I item 5) *Item level cut-off point of 2*	209	$\chi^2(1)=.04$	$p=.83$	.01
Fatigue (PHQ-9 item 4, dichotomized and SCID-I item 6) *Item level cut-off point of 2*	206	$\chi^2(1)=13.78$	**$p < .001$	.25
Feeling bad about oneself (PHQ-9 item 6, dichotomized and SCID-I item 7) *Item level cut-off point of 2*	208	$\chi^2(1)=3.67$	$p=.056$	.13
Concentration PHQ-9 item 7, dichotomized and SCID-I item 8) *Item level cut-off point of 2*	209	$\chi^2(1)=3.66$	$p=.056$	.10
Suicide (PHQ-9 item 9, dichotomized and SCID-I item 9) *Item level cut-off point of 1*	208	$\chi^2(1)=26.17$	**$p < .001$	.35
Item level cut-off point of 2	208	$\chi^2(1)=12.06$	*$p=.001$	.16

* Significant at $p < .05$.
** Significant at $p < .001$.

anhedonia scores as the predictor was statistically significant, $\chi^2(1) = 42.26$, $p < .001$ (Nagelkerke's $R^2 = .12$). The proportion of cases accurately predicted was 70.40%. Each increase of 1 unit in the PHQ-9 item was associated with a 1.69 times greater likelihood of endorsing the relevant anhedonia SCID item.

Further, we examined the relationship between the remaining PHQ-9 items with the corresponding SCID-I items using chi-square analyses. The sample size for each of the final seven PHQ-9 items varied because of occasional missing values. The item level cut-off score of "2" was again used for positive endorsement. The chi-square values with significance levels, kappa coefficients and sample sizes for each of the seven PHQ-9 items are shown in Table 2. Results indicated significant associations for the items representing appetite changes, sleep changes, fatigue and suicidal ideation. Further, items representing feeling bad about oneself, and concentration difficulties had close to significant associations ($p = .056$), with a chance of significance with a larger sample size. Additionally, an analysis of the PHQ-9 item of suicidal ideation using the cut-off score of one and above as positively endorsed and the corresponding SCID-I items (Table 2) indicated a significant association.

To assess the predictive relationship between total PHQ-9 scores and MDE criterion A, MDE, and MDD based on the SCID-I scores we computed logistic regression and receiver operating characteristic curve analyses. For MDE criterion A based on the SCID-I scores, results indicated that PHQ-9 total scores were statistically significant, $\chi^2(1) = 130.36$, $p < .001$ (Nagelkerke's R^2 of .34, correct classification = 81.10%). Each increase of 1 unit in PHQ-9 total scores was associated with a 1.22 times greater likelihood of meeting MDE criterion A. For MDE diagnosis based on the SCID-I responses, results indicated that PHQ-9 total scores were statistically significant, $\chi^2(1) = 121.21$, $p < .001$ (Nagelkerke's R^2 of .32, correct classification was 81.10%). Each increase of 1 unit in PHQ-9 total scores was associated with a 1.21 times greater likelihood of meeting criteria for MDE per SCID-I scores. For an MDD diagnosis based on SCID-I scores, results indicated that PHQ-9 total scores were statistically significant, $\chi^2(1) = 96.64$, $p < .001$ (Nagelkerke's R^2 of 27, correct classification was 83.50%). Each increase of 1 unit in the PHQ-9 total score was associated with a 1.19 times greater likelihood of meeting the criteria for MDD.

Nonparametric ROC curve analyses indicated that PHQ-9 total scores have moderate accuracy in detecting people who (a) met MDE criterion A ($AUC = .80$, $SE = .02$, $p < .001$), (b) met criteria for MDE ($AUC = .80$, $SE = .03$, $p < .001$), and (c) met criteria for MDD ($AUC = .78$, $SE = .03$, $p < .001$). The accuracy criteria for ROC curves are per recommended guidelines (Fischer et al., 2003).

Table 3
Diagnostic efficiency statistics the PHQ-9 using SCID-I as the gold standard.

	Sensitivity	Specificity
PHQ-9 lifetime MDE		
SCID I lifetime MDE A	0.358	0.950
SCID I lifetime MDE diagnosis	0.355	0.941
SCID lifetime MDD	0.383	0.938
PHQ-9 total score of $>/=10$		
SCID I lifetime MDE A	0.557	0.858
SCID-I lifetime MDE	0.561	0.848
SCID-I lifetime MDD	0.542	0.828
PHQ-9 total score of $>/=15$		
SCID-I lifetime for MDE A	0.351	0.964
SCID-I lifetime MDE	0.371	0.962
SCID-I lifetime MDD	0.392	0.956
PHQ-9 total score of $>/=20$		
SCID-I lifetime MDE A	0.106	0.994
SCID-I lifetime MDE	0.115	0.994
SCID-I lifetime MDD	0.121	0.992

Note. MDE refers to major depressive episode and MDD refers to major depressive disorder.

Diagnostic efficiency statistics, specifically sensitivity and specificity of the PHQ-9 diagnostic algorithm and specific cutoff scores (10, 15 and 20) for the SCID-I depression designations are reported in Table 3. Overall, specificity statistics were better than the sensitivity statistics. Using the PHQ-9 lifetime diagnosis algorithm, sensitivity ranged from 0.355 to 0.383 and specificity ranged from 0.938 to 0.950. Further, using a PHQ-9 cut-off score of 10 and beyond, sensitivity ranged from 0.542 to 0.561 and specificity ranged from 0.828 to 0.858. With a PHQ-9 cut-off score of 15 and beyond, sensitivity ranged from 0.351 to 0.392 and specificity ranged from 0.956 to 0.964. Lastly, with a PHQ-9 cut-off score of 20 and beyond, sensitivity ranged from 0.106 to 0.121 and specificity ranged from 0.992 to 0.994.

4. Discussion

These results support the use of the telephone administered PHQ-9 as a measure of lifetime MDE Criterion A, MDE diagnosis, and an MDD diagnosis. The results confirm a significant relationship between six of the PHQ-9 and SCID-I items using the item-level cut-off score of two for the PHQ-9 items. We also found a predictive relationship between total PHQ-9 scores and MDE Criterion A, MDE diagnosis, and an MDD.

Our study found a significant associative and predictive relationship between the first two cardinal items of the PHQ-9 and SCID-I using the item-level cut-off score of two for the PHQ-9 items. Further, the degree of agreement per Kappa coefficients was fair (Landis and Koch, 1977). The proportion of cases positively endorsing the SCID-I cardinal items correctly identified by the PHQ-9 using two as the cut-off point were approximately 70%, reflecting the utility of the cardinal items as screening items.

The results from a similar relational analysis between the final seven items of the PHQ-9 and SCID-I revealed four out of seven items significant. Using an item level cut-off point of "1" or "2", the suicidal ideation item of the PHQ-9 was significantly associated with its SCID-I counterpart, with better agreement when using an item-level cut-off point of "1", which is consistent with the scoring recommendations (Kroenke et al., 2001). Using "2" as the cut-off point, the appetite, sleep changes and fatigue items of the PHQ-9 were significantly associated with the SCID-I counterparts. The PHQ-9 items representing feeling bad about oneself and concentration difficulties were close to but did not reach significance. The item assessing motor activity was not significantly associated with the SCID-I counterpart using the recommended item-level cut-off point.

Our study found that most of the PHQ-9 items performed adequately when compared to the SCID-I items. Given that the two PHQ-9 items of feeling bad about oneself, and concentration difficulties almost corresponded accurately with the SCID-I item counterpart at an item-level cut-off point of two, further research, using a larger dataset, might reveal a significant association. The item representing motor activity does not have a significant correspondence with the SCID-I counterpart, thus raising the question of its utility. However, it needs to be noted that the SCID-I specifically searches for the worst depressive episode while the PHQ-9, as administered in this study, did not. This may have resulted in persons reporting fewer and weaker symptoms in the PHQ-9 telephone interview, contributing to the lack of correspondence between these three items.

We demonstrated the predictive relationship between total PHQ-9 scores and MDE Criterion A, MDE diagnosis, and an MDD diagnosis with cases correctly identified approximately 80% of the time. Further, ROC analysis revealed that the accuracy of the PHQ-9 in detecting MDE Criterion A, MDE, and MDD was moderate. The trend was that higher PHQ-9 scores result in a greater accuracy in

prediction, but with reduced sensitivity that could result in missing many true positives. This would be a significant weakness if the PHQ-9 telephone administrations were used for clinical purposes.

We showed that the cutoff point of 10 performed better than the diagnostic algorithm for a PHQ-9 based diagnosis. Overall specificity statistics were better than the sensitivity statistics, meaning that the PHQ-9 has better ability to detect negative cases rather than positive cases. Our study found lower sensitivity ratings for the telephone administered PHQ-9 compared to what is found in prior literature utilizing the self-report administered PHQ-9 (Arroll et al., 2010; Kroenke et al., 2001; Wittkampf et al., 2009). In terms of the recommended cut-off score, it appears that the cut-off score of 10 resulted in the highest sensitivity (range .542–.561), however yielded the lowest specificity (range .828–.858). Utilizing either the PHQ-9 diagnostic algorithm or the higher cutoff scores raised specificity and lowered sensitivity, confirming similar results (Cannon et al., 2007). Additionally, using the cutoff score of 10, the telephone interview prevalence of lifetime MDE (25.10%) was closest to that found by the in-person interview using the SCID (24.3%), with the prevalence of lifetime MDE using the diagnostic algorithm falling to 13.10% (roughly half the prevalence found by the SCID-I). Thus, the cut-off point of 10 is recommended for an optimal balance between sensitivity and specificity compared to other cut-off scores or the diagnostic algorithm, confirming the proposed hypothesis. For clinical purposes a cutoff of 10 may be best for being most inclusive in evaluating patients, while for epidemiological purposes specificity is more important than sensitivity so the algorithm approach may be better.

Overall, the results of the current study provide support for the telephone administration of the PHQ-9 to assess the lifetime prevalence of MDE and MDD in a non-clinical population, with several clinical and research implications. First, for maximum sensitivity and specificity, it is recommended using 10 as the cut-off point compared to the other cut-off points or the diagnostic algorithm in a non-clinical population. Second, considering the good predictive relationship of the PHQ-9 total scores for MDE and MDD based on the SCID-I scores, one could use the shorter, quicker, and telephone-administered PHQ-9 for research purposes. This is a good alternative to a more time consuming and more training intensive SCID-I administration, and provides the ability to screen for depression over the phone expanding geographical accessibility, increasing flexibility and ease of administration, reducing financial costs, and increasing response rates. Lastly, the PHQ-9 can be used to assess lifetime MDE and MDD by adjusting the timeline for the assessed symptoms. However, the idea that it is a screening instrument needs to be kept in mind, and if positive, needs to be followed by a thorough clinician-administered depression assessment like the SCID-I.

Limitations of this study include several factors. Our study sample had a slightly higher base rate of the MDD and MDE diagnoses than in a representative community sample. Also, the time difference between the administrations of the PHQ-9 and SCID-I (approximately three months) could have affected the results. The wording of our modification of the PHQ-9 to assess lifetime depression did not specifically instruct participants to report the "worst episode" as is sought when the SCID is administered which could have resulted in participants reporting fewer and weaker symptoms on the PHQ-9. Additionally, the study uses a population based sample of military veterans which may limit its applicability to other populations.

The results have implications for future research. Given the potential of the telephone administered PHQ-9 as a valuable depression-screening instrument it could be validated in a similar manner using clinical populations. Also, research validating the telephone-administered PHQ-9 could explore possible differences emerging from gender, educational level, or age, which would prove valuable for both research and clinical use. Future research could explore the differences between lay telephone interviewers and clinician telephone interviewers. The telephone administered PHQ-9 is a valuable tool for both research and clinical purposes, and it is worthwhile to continue to refine our understanding of its application.

Conflict of interest

Joseph R. Calabrese, M.D. discloses the following financial interests. Non-CME: Benecke,lundbek,Medwiz Health Care, Promedica, Spirant Communication Private Limitex.

Consulting: Biomedical Development Corporation, Convergent Health Solutions, Elan, Health and Wellness, Hoffman Laroche, Lundbeck, Otusuka, Scientia, Sunovian, Takeda, Teva.

Academia: Ohio Psychiatric Association, Ohio State University, University of Cincinnati, University of Toronto.

All other authors declare that they have no conflicts of interest.

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Brief report

Smoking is a predictor of depression onset among National Guard soldiers

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ARTICLE INFO

ABSTRACT

This report examines the relationship between smoking and depression in a sample of American soldiers. Persistent, active smoking is associated with increased risk of incident depression at follow up. History of smoking in the absence of current smoking at baseline was not associated with depression at follow-up.

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1. Introduction

Major depression is increasingly recognized as a serious health problem among military personnel in the United State (Tanielian and Jaycox, 2008). The National Guard is a subgroup of the US military among whom rates of depression are even higher than among active military personnel (Thomas et al., 2010). Several reports suggest that smoking is also disproportionately common among military service personnel (Schei and Søgaard, 1994; Bray et al., 2010), although this varies to some degree by age and unit of service. Cigarette smoking has a long history of being tolerated and even encouraged in American military culture (Conway, 1998; Smith and Malone, 2009). Trend data show that over the past 28 years cigarette smoking in the US military has decreased. However, the prevalence of cigarette smoking remains high among military personnel with some estimates reporting that up to 31% of active duty military personnel are current smokers (Department of Health and Human Services, 2011).

Recently several general population studies have documented a link between smoking and increased risk of depression (Breslau et al., 1991; Fergusson et al., 2003; Boden et al., 2010; dos Santos et al., 2010; Kang and Lee, 2010). Several studies have documented

relationships between depressive symptoms, suicide behavior, stress and high levels of tobacco use among military populations (Miller et al., 2000; Gulec et al., 2005; Bray et al., 2010). With the exception of one previous study of Turkish medical military undergraduates that found a relationship between smoking and depression (Gulec et al., 2005), studies among military populations have not directly examined the relationship between depression and smoking. Against this background, this study assessed the relationship between depression and smoking in a sample of National Guard members. We hypothesized that this relationship would be significant, and even stronger than in the general population, given the disproportionate burden of stress and cigarette smoking among military populations.

2. Methods

2.1. Study population and survey

Data were drawn from the Ohio Army National Guard Health Initiative (OHARNG MHI). The OHARNG MHI is a longitudinal cohort of Ohio Army National Guard Soldiers who are interviewed annually to assess mental health, substance use and life experiences. All enlisted soldiers between June 2008 and February 2009 with a current address ($N=12,225$) were notified that they may be contacted to participate in a telephone interview; 1013 opted to be non contacted further (8.3%). Of the remaining 11,212 soldiers, 58.1% had contact information and thus were possible participants ($n=6514$). This group was further reduced to a final baseline sample of 2616 after eligibility, language proficiency, and desire to participate were taken into account; the overall survey response rate was 43.2%. This was calculated as those who consented to an interview ($N=187$ retired$+2616$ completed) over all possible participants ($N=6514-31$ ineligible

as heard of hearing or non-English speaking). Participants were contacted for follow-up interviews in November of 2009, within 12 months of their original interview, and given 12 months to respond. 67.7% of the original 2616 soldiers responded to follow-up surveys (n=1770). This study included the 1770 soldiers who participated in both baseline and follow-up surveys. After giving written, informed consent, soldiers participated in computer-assisted telephone interviews that obtained information on mental health, substance use, military experiences, and life events history. The investigation was carried out in accordance with the latest version of the Declaration of Helsinki. The study design was reviewed by University of Michigan and Case Western IRB and informed consent of the participants was obtained after the nature of the procedures had been fully explained.

2.2. Measures

The main independent variable of interest was whether or not an individual reported smoking at baseline. The main dependent variable of interest was depression status at time 2. The Patient Health Questionnaire-9 (PHQ-9) was used to evaluate depression (Kroenke et al., 2001). Incident depression at time 2 was defined as having at least two out of nine symptoms at follow-up and they must have occurred between the baseline survey and follow-up survey among participants with no history of depression at baseline (individuals had to have at least two co-occurring symptoms at some point in the past to be considered to have a history of depression at baseline) (Kroenke et al., 2001). A concurrent clinical reappraisal was conducted with the OHARNG MHI baseline survey and found the PHQ-9 to be highly specific (98%) with moderate sensitivity (58%) as compared to clinician-administered interviews (Calabrese et al., 2011). With high specificity and moderate sensitivity, the CATI administered PHQ-9 removes virtually all false positive depressed participants. Other covariates included smoking status at follow-up, age and gender. Age was included as an indicator variable (18–24 (reference group), 25–34, 35–44, 45+).

2.3. Statistical analysis

For the study sample, those who did not answer the smoking series of questions were eliminated (N=4) and only those who were at risk for incident depression at follow-up were included (N=1391). To be considered at risk, those who ever had a history of depression as reported in the baseline survey were excluded (375). Within this sample, the distribution of incident depression was examined among those who were and were not smoking. The distribution of incident depression among the multiple categories of smoking (never, history but not currently, on and off again, incident smoker, chronic smoker) was then examined. Using unadjusted logistic regression, the crude association between smoking status and incident depression was estimated. Adjusted logistic regression was then used to estimate the crude association between smoking status and incident depression adjusting for age and gender.

3. Results

The distribution (number (%)) and the association (crude odds ratio, 95% CI) of depression at follow-up according to the baseline and follow-up characteristics are listed in Table 1. The majority of the sample was male (87.6%) and below the age of 35 (64.9%). In bivariable cross-sectional associations, smoking status at baseline was associated with depression at baseline. History of smoking (but not current) (AOR=1.2 (0.7, 2.1)), sporadic/inconsistent smoking

(AOR=2.2 (0.9, 5.2)) and incident smoking (AOR=2.7 (0.6, 12.4)) at baseline were not associated with increased risk of depression at follow-up but chronic smoking was associated with significantly increased risk of incident depression at follow-up (AOR=2.0 (1.2, 3.4)). This association remained statistically significant after adjusting for demographic differences.

4. Discussion

The first study of the relationship between smoking and depression over time among military personnel found that persistent smoking is associated with incident depression among National Guard soldiers. This finding is consistent with results from several longitudinal studies showing that smoking is associated with increased risk of depression in general population samples (Covey et al., 1998; Boden et al., 2010; dos Santos et al., 2010; Kang and Lee, 2010).

There are four main explanations for the observations noted here. First, while the military has traditionally experienced higher rates of smoking than the general population, recently there have been targeted efforts to improve smoking cessation in the military (Bondurat and Wedge, 2009). Therefore, it is conceivable that depression could result from increased exposure to stigma among remaining smokers though this seems less likely in the military than among some other population subgroups. Second, there is a near-perpetual state of withdrawal among chronic smokers, beginning after the effects of the last cigarette wear off. Since soldiers are frequently unable to smoke at will while fulfilling their duties, it is possible that they are more vulnerable to depression via increased exposure to withdrawal symptoms than the civilian population. Third, it is possible that smoking influences the brain through depletion of serotonin due to frequent nicotine use, leading to increased vulnerability to depression via neurobiological pathways (Malone et al., 2003). Fourth, the relationship between smoking and depression among National Guard members could result from uncontrolled confounding. For example, anxiety disorders, substance use disorders (i.e. alcohol and illicit substances) and exposure to traumatic events are all associated with increased smoking and depression (Vlahov et al., 2002; Kalman et al., 2005; Feldner et al., 2007). It is possible that exposure to one of these factors results in the observed association.

Limitations of this study should be considered. First, while levels of smoking were examined at two time points, there was no measure of nicotine dependence. Future studies that can differentiate between dependent and non-dependent smoking, including an examination of withdrawal symptoms in the relationship between smoking and depression will lead to a better understanding of the relationship between smoking and depression in the military. Second, fairly small cell sizes did not allow

Table 1
Smoking characteristics among those at risk for depression and association between smoking status and depression.

Smoking status	Total	Incident occurrence of depression	Crude odds ratio (95% CI)	Adjusted[a] odds ratio (95% CI)
Smoked at baseline				
No	995 (71.5)	61 (6.1)	1	1
Yes	396 (28.5)	37 (9.3)	1.6 (1.0, 2.4)	1.7 (1.1, 2.5)
Categories of smoking				
Never smoked	586 (42.1)	31 (5.3)	1	1
History of smoking but not currently	366 (26.3)	24 (6.6)	1.3 (0.7, 2.2)	1.2 (0.7, 2.1)
On and off smoker	71 (5.1)	7 (9.9)	2.0 (0.8, 4.6)	2.2 (0.9, 5.2)
Incident smoker	19 (1.4)	2 (10.5)	2.1 (0.5, 9.5)	2.7 (0.6, 12.4)
Chronic smoker	349 (25.1)	34 (9.7)	1.9 (1.2, 3.2)	2.0 (1.2, 3.4)

CI, confidence interval.

[a] Models were adjusted for age and gender.

adjustment for a number of potential confounders (e.g., exposure to traumatic experiences, substance use disorders, other mental disorders). Yet, numerous previous studies have examined potential confounders and the relationship has remained significant.

The current study provides evidence that smoking is associated with incident depression, and provides the first evidence of a relationship between smoking and depression among National Guard members. As smoking continues to be highly prevalent among military personnel, these data suggest the burden of mental health – as well as physical health – consequences of smoking. As such, the importance of making smoking cessation programs available to soldiers—as prevention of subsequent mental health problems, as well as a means to stop smoking—cannot be overestimated.

Author disclosure

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Validation of lay-administered mental health assessments in a large Army National
Guard cohort

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Abstract

Purpose: To report the reliability and validity of key mental health assessments in an ongoing study of the Ohio Army National Guard (OHARNG).

Methods: 2616 OHARNG soldiers received hour-long structured telephone surveys including the Posttraumatic Stress Disorder (PTSD) Checklist (PCL-C) and Patient Health Questionnaire – 9 (PHQ-9). A subset (N=500) participated in 2 hour clinical reappraisals, using the Clinician-Administered PTSD Scale (CAPS) and the Structured Clinical Interview for DSM (SCID).

Results: The telephone survey assessment for PTSD and for any depressive disorder were both highly specific [92% (SE 0.01), 83% (SE 0.02)] with moderate sensitivity [54% (SE 0.09), 51% (SE 0.05)]. Other psychopathologies assessed included alcohol abuse [sensitivity 40%, (SE 0.04) and specificity 80% (SE 0.02)] and alcohol dependence [sensitivity, 60% (SE 0.05) and specificity 81% (SE 0.02)].

Conclusion: The baseline prevalence estimates from the telephone study suggest alcohol abuse and dependence may be higher in this sample than the general population. Validity and reliability statistics suggest specific, but moderately sensitive instruments.

Key Words: military, assessment, "posttraumatic stress disorder", "depressive disorders", "alcohol use disorders"
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Introduction

The link between combat exposure and psychopathologies, including posttraumatic stress disorder (PTSD), depression, anxiety, and substance abuse among military populations is well documented (Johnson *et al.*, 2009; Killgore *et al.*, 2006). Studies suggest that between 4.8-18% of military populations have had PTSD at some point in their lifetimes (Dohrenwend *et al.*, 2006; Hoge *et al.*, 2004; Iversen *et al.*, 2009; Vasterling *et al.*, 2006) compared with a 6.8-9.2% lifetime prevalence of PTSD for the general United States population (Breslau *et al.*, 1998; Kessler *et al.*, 2005a). Similarly, studies suggest that military personnel have a greater lifetime prevalence of depression and generalized anxiety compared with the general population (Hoge *et al.*, 2004; Kulka, 1990).

During Operation Iraqi Freedom (OIF) and Operation Enduring Freedom (OEF) the National Guard and Reserve forces were deployed to combat zones at an unprecedented level (Vogt *et al.*, 2008) and in 2007 comprised approximately 27% of the total troops deployed in Operation Iraqi Freedom (OIF) and in Operation Enduring Freedom (OEF)(Sollinger *et al.*, 2008). Little is understood about the long-term effects of deployment on National Guard soldiers compared to their active duty counterparts. Some studies suggest that Guard soldiers may be at greater risk of deployment stressors and adverse mental health effects of war than active duty soldiers (Smith *et al.*, 2008; Sollinger *et al.*, 2008). For example, Guard soldiers deployed to conflict areas are exposed to the same combat experiences as active duty personnel but face different deployment stressors including maintaining a civilian job while deployed and deploying with a unit with which they did not train (Hotopf *et al.*, 2006; La Bash *et al.*, 2009; Vogt *et al.*, 2008). Additionally, National Guard veterans face different stressors upon returning home including limited access to healthcare compared to active duty soldiers (Milliken *et al.*, 2007). Milliken et al. [2007] screened soldiers 6 months after their return from Iraq and found that, compared with active duty forces, twice as many reserve members required referral for mental health problems. As we approach the end

of OEF and OIF and given the lack of understanding about how deployment affects reserve forces overtime, there is a need to document mental health over time in the National Guard population.

Assessment of mental health conditions by trained clinicians is considered the gold standard but is costly and logistically challenging within large population-based studies (Smith *et al., 2007).* As a result, cohort studies of mental health have historically employed more practical interview methods including web-based self-report surveys as conducted by the Millennium Cohort, a large US military cohort (Smith *et al., 2007a;* Smith *et al., 2007b),* or telephone-based interviews as conducted by the CDC Behavioral Risk Factor Surveillance System (Remington *et al.*, 1988).

The Ohio Army National Guard Mental Health Initiative (OHARNG MHI) is a longitudinal study that annually monitors the factors associated with and course of mental health within a representative sample of service members from the Ohio Army National Guard (Calabrese *et al.*, 2011; Goldmann *et al.*, 2012). We report here the psychometrics of the structured mental health assessments completed with a computer-assisted telephone interview as compared to gold-standard of clinical face-to-face interviews.

Methods

Study Population and Sampling
The study population of the OHARNG MHI is the OHARNG soldiers who served in the Guard between June 2008 and February 2009; the final study sample is 2616 randomly selected OHARNG soldiers [men and women, 18 years or older (with some 17 year old emancipated minors) of any ethnicity and capable of informed consent]. OHARNG soldiers were invited to participate through a process that included, first, a letter alerting soldiers of the study with an option to opt-out and, second, a phone call to obtain each soldier's consent to participate in a telephone interview.

During the first stage of enrollment, all soldiers enlisted in the OHARNG between June 2008 and February 2009 received alert-letters directly from the OHARNG (N=12,225 excludes the 345 without an address). Of all guard soldiers who received the alert-letters, 8% (1013 soldiers) returned opt-out cards to the OHARNG.

During the second stage of enrollment, we contacted possible participants to obtain informed consents for the telephone interviews. If the service member was deployed at the time of contact, information was requested on when the member would return and a call was scheduled. If after 10 telephone calls for a 2 week period at different times of the day and contact was unsuccessful, a non-contact letter was sent to the possible participant's address in an attempt to obtain a working telephone number.

The consent procedure and survey were piloted in November 2008 with 15 service members using a computer-assisted telephone interview (CATI). Official enrolment began in December 2008 and continued through the end of November 2009 when the desired sample size was reached. Participants were compensated for their time.

Clinical re-appraisal

We also conducted clinical reappraisals on a sub-sample of the telephone survey participants. At the end of the initial telephone interviews, a random sample of 500 participants participated in the in-depth clinical interview. In person interviews were conducted by Doctoral and Masters level clinicians, took place in a setting familiar to the participant, averaged 2 hours, and participants were compensated for their time.

Assessment Instruments

The OHARNG Mental Health Initiative CATI included questions on lifetime experiences, deployment and military experiences, current living situation, and past and present symptoms of psychopathology.

Psychopathologies were assessed using standardized and well-validated scales. The Posttraumatic Stress Disorder (PTSD) Checklist (PCL) (Blanchard *et al.*, 1996) was

used to collect PTSD symptoms in relation to participants' self-identified "worst" event experienced both outside and during their most recent deployments (Blake *et al.*, 1995; Hoge *et al.*, 2004; Weathers *et al.*, 1999). Questions were added to assess additional criteria for PTSD diagnosis as listed in the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) ("Diagnostic and Statistical Manual of Mental Health Disorders", 2000). To have had PTSD, a person had to experience criterion A1 and A2 (experience a traumatic event and intense fear, hopelessness or horror due to a trauma); criterion B where at least 1 symptom of re-experiencing the trauma was reported; criterion C where at least 3 symptoms of avoidance of the trauma were reported; criterion D where at least 2 symptoms of increased arousal were reported; criterion E where symptoms lasted for at least 1 month; and criterion F where the symptoms caused significant impairment ("Diagnostic and Statistical Manual of Mental Health Disorders", 2000; Weathers *et al.*, 1991).

To assess depressive episodes and obtain occurrence of suicidal ideation, we used the Primary Care Evaluation of Mental Health Disorders Patient Health Questionnaire – 9 (PHQ-9) (Kroenke *et al.*, 2001). To have had a major depressive disorder (MDD), the participant had to report ≥ 5 of 9 symptoms on the PHQ-9 and symptoms had to occur together within a 2-week period along with either depressed mood or anhedonia. We also examined a more inclusive definition of depression defined by those who, within a 2 week period with either depressed mood or anhedonia, scored ≥ 2 out of 9 symptoms on the PHQ-9 (Kroenke *et al.*, 2001). Suicidal ideation was assessed through the PHQ-9 question asking whether participants had thoughts of death or wanting to hurt themselves within the past 30 days (Kroenke *et al.*, 2001).

GAD was assessed with the Generalized Anxiety Disorder – 7 (GAD-7) (Spitzer *et al.*, 2006). A probable case of GAD was classified as a score ≥ 10 on the GAD-7, duration of symptoms at least 6 months, reported functional impairment, with symptoms grouped

together (Spitzer *et al.*, 2006). As the clinical re-appraisal interview only captured current cases, we only examined current cases of GAD in the past 30 days.

The Mini International Neuropsychiatric Interview (MINI) and DSM-IV criteria were used to assess alcohol dependence and alcohol abuse (Sheehan *et al.*, 1998). Participants with lifetime alcohol abuse ever in lifetime met DSM-IV criterion 1 (at least 1 symptom of maladaptive pattern of substance use leading to clinically significant impairment or distress) and criterion 2 (symptoms never met the criteria for alcohol dependence) ("Diagnostic and Statistical Manual of Mental Health Disorders", 2000; Sheehan *et al.*, 1998). Those with alcohol dependence ever in lifetime met at least 3 symptoms of maladaptive pattern of alcohol use leading to clinically significant impairment or distress ("Diagnostic and Statistical Manual of Mental Health Disorders", 2000; Sheehan *et al.*, 1998).

Clinical reappraisal instruments

For the clinical reappraisal, the Clinician-Administered PTSD Scale (CAPS) was used to assess PTSD based on the "worst" event outside of their deployments as well as the "worst" event during any deployment; deployment events were not limited to the most recent deployment as with the telephone interview (Blake *et al.*, 1995; Weathers *et al.*, 1999). The diagnosis of PTSD for the clinical reappraisal was based on the scoring rules outlined by Weathers, et al [1999] for the CAPS and followed the DSM-IV algorithm ("Diagnostic and Statistical Manual of Mental Health Disorders", 2000; Blake *et al.*, 1995; Weathers *et al.*, 1999). To have a positive symptom for DSM-IV PTSD criteria B – D, a participant had to have a frequency ≥ 1 per symptom (at least once or twice in their lifetime) as well as a symptom intensity of ≥ 2 (at least moderate -- distress clearly present but still manageable and some disruption of activities). To be diagnosed with PTSD a participant had to have all criteria from the DSM-IV (A-F)

The diagnoses for lifetime occurrence of MDD, alcohol abuse and alcohol dependence, and current occurrence of GAD were based on the Structured Clinical Interview for

DSM-IV-TR (SCID) Axis I Disorders (non-patient version) and DSM-IV criteria ("Diagnostic and Statistical Manual of Mental Health Disorders", 2000; First, 2002).

Suicidal ideation was evaluated using MINI Plus (Sheehan *et al.*, 1998). A positive response was a score of at least 'moderately' (9 points or greater) on the question of suicide attempts in the past 6 months.

Statistical Methods

First, we compared the distribution of demographic characteristics (e.g., age, gender, and education) from those in the baseline sample (telephone survey (N=2616)) and those later selected to participate in the clinical reappraisal (N=500) using chi-square tests.

Second, the lifetime prevalence of each psychopathology – PTSD, MDD, other forms of depression, GAD (past 30 days), alcohol abuse, alcohol dependence, and suicidal ideation (past 30 days)– was described for the entire baseline sample.

Third, we examined the validity and reliability of the telephone assessments compared with the clinical reappraisal. Using the 500 participants who were in both samples, we applied 4 tests of validity and 3 tests of reliability following methods presented by Kessler et al [2005b] in the National Co-morbidity Survey Replication (NCS-R) (Kessler *et al.*, 2005b).

To assess validity and using the clinical reappraisal as the gold standard, we calculated the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) for all psychopathologies. Next, using the overall continuous score from each of the psychopathology scales, we examined the area under the curve (AUC) as a measure of overall accuracy based on the continuous score of the telephone assessment and the gold standard of the clinical interview. All standard errors reported were asymptotic.

To assess reliability, we calculated the kappa statistic and the McNemar's statistic between diagnoses according to the telephone interview and clinical reappraisal. The final measure of reliability was Cronbach's alpha applied to the telephone survey questions.

Finally, to test whether disease misclassification between the telephone and the clinical reappraisal depended on participant characteristics, we compared the sensitivity and specificity for each psychopathology calculated separately for men and women, participants < 35 and ≥ 35 years of age, and white and non-white categories. Confidence intervals (CI) for these statistics were asymptotic unless the sample size was ≤ 50, in which case exact CIs were reported.

All analyses were carried out with SAS 9.2.

Results

Of the 11,212 soldiers for whom contact information was received from the Guard, 10.1% (1130) were excluded because they did not have a listed telephone number or address and 31.8% (3568) were excluded due to non-functioning or incorrect numbers and not returning a non-contact letter (Figure 1). Of the 6514 possible participants with working numbers (58.1% of the original telephone number list), only 20.9% (1364) declined to participate and 36.0% (2347) were not included because they were not enrolled before the baseline cohort closed in November 2009 (n=2316) or disqualified for other reasons (e.g., did not speak English, hearing problems, or deceased, n=31). 187 were retired and therefore ineligible. Overall, our participation rate was 43.2% calculated as those who completed the telephone survey plus those who would have consented had they not been retired divided by all of the working numbers minus those disqualified for other reasons.

There were no differences between the characteristics of the baseline and clinical reappraisal samples (Table 1). The majority of participants were male (85.2%), white

(87.7%), and non-officers, including enlisted soldiers, cadets, or civilian employees (86.9%). The majority had some form of deployment/mobilization experience (35.9% never deployed in the baseline sample); 30.3% of the sample were most recently deployed to a conflict setting.

Table 2 lists the prevalence of each condition in the total baseline sample. The most commonly reported lifetime condition was alcohol abuse (24.0%) followed by alcohol dependence (23.5%). 10.3 % of the sample had MDD at some point in their lives and 21.4% had some form of depression (MDD including other forms of depression). Deployment-related PTSD was reported by 7.4% of the telephone sample while 9.6% had PTSD ever in lifetime. GAD (1.7%) and suicide risk (1.9%) were rarely reported

For the validity measures (Table 3), specificity and NPV were higher than sensitivity and PPV for all diagnoses. The telephone diagnosis was most sensitive for alcohol dependence (0.60) and least sensitive for GAD (0.04). The telephone diagnosis was most specific for GAD (0.98) and least specific for alcohol abuse (0.80). The PPV varied but was moderate to low for all conditions, the highest being for MDD (0.64). The NPV was very high for all conditions, the lowest being for alcohol abuse (0.77). Reliability statistical testing results (Table 3) produced relatively moderate kappa values, for example, 0.34 for PTSD ever in lifetime and 0.37 for alcohol dependence. McNemar's test rejected the null hypothesis of no marginal heterogeneity between the telephone sample and clinical interview subsample for PTSD, MDD, GAD, and alcohol dependence. The measure of reliability and internal agreement for the telephone psychopathologies reported by Cronbach's alpha ranged from 0.95 for deployment-related PTSD to 0.57 for alcohol abuse.

The sensitivity and specificity of the telephone diagnoses stratified by gender, age, and race across the psychopathologies showed no misclassification related to these demographic variables (Table 4). There was evidence of misclassification for alcohol

abuse by gender; the sensitivity and specificity for alcohol abuse was higher for men than women.

Discussion

Overall, the validity and reliability statistics for the computer assisted telephone psychopathology assessment indicated that the methods performed well as research instruments for research on PTSD, depression, alcohol abuse, and suicide risk.

All structured screening instruments had high specificity, a necessary characteristic in order to accurately estimate population prevalences (Terhakopian *et al.*, 2008). The sensitivity and specificity for nearly all of the psychopathology diagnoses in the telephone sample did not differ by demographic group, suggesting there was not differential misclassification. This implies that any misdiagnoses for these conditions are random, rather than based on participant characteristics. There was, however, some suggestion that alcohol abuse may be misclassified by gender; women were less likely to be correctly diagnosed than men. Given the high specificity and moderate sensitivity, telephone assessments will be particularly important in the long-term for population assessments and research tools. They will not, however, replace traditional methods of screening for individual treatment.

The telephone assessments had moderate to high levels of reliability across the three measures assessed: kappa, Cronbach's alpha, and McNemar's test. The kappa statistics were fair for suicide risk and all diagnoses with the exception of GAD, suggesting that agreement between the telephone and clinical diagnoses was not due to chance, other than possibly for GAD (Table 3). However, the statistics for GAD showed good internal consistency. Spitzer [2006] reported a Cronbach alpha of 0.92 for his GAD validation study, higher than ours (0.72), but comparable (Spitzer *et al.*, 2006). The other Cronbach alphas in Table 3 also indicate consistency and that the index questions represented the same underlying construct.

Lastly, for McNemar's test of reliability, the finding that psychopathology diagnostic results for several conditions did not reject the null of marginal homogeneity suggested that the telephone assessment and clinical interview were using the same core criteria for diagnoses of alcohol abuse, any depressive disorder, and suicide risk. In comparison, PTSD, MDD, GAD, and alcohol dependence tests rejected the null of marginal homogeneity, suggesting some differences in the core diagnostic criteria between the telephone and the clinical interview subsample. As the MDD diagnosed on the telephone compared to the clinical interview varied, we compared the general depression (including MDD and other forms of depression) prevalence from the telephone sample with MDD in the clinical interview subsample. We found these two diagnostic tests were more reliable and appeared to use the same diagnostic criteria. It is of note that in the NCS-R, Kessler, et al [2005b] reported comparable reliability statistics for these psychopathologies. However, Kessler et al found core diagnostic differences by McNemar's test between the World Health Organization Composite International Diagnostic Interview (CIDI) and the SCID for PTSD, MDD, alcohol abuse, and alcohol dependence, whereas we found differences for PTSD, MDD, GAD, and alcohol dependence.

Reliability statistics are population dependent, so it is important to understand that the findings from this military population study may not be generalized to other populations. The current study is also limited by the small percentage of women and other minorities; however, the demographics of our sample very closely mirror the overall demographics of the OHARNG. Future work should also compare the item-by-item response of the telephone assessments to the clinical interview assess if there are internal differences within a construct.

This work suggests that the computer assisted telephone psychopathology assessments used in the OHARNG MHI are valid and reliable research tools for the National Guard population. As compared to face-to-face interviews, the telephone assessments may also prove to be more cost-effectiveness based on the reduced cost

of travel for such a widespread population (N=2616). Our telephone assessments had comparable, if slightly lower, measures of reliability as compared to the MILCO study web-based interviews (Smith *et al.,* 2007a). The web-based interviews from the MILCO study, however, resulted in a slightly lower response rate (37%) as compared to the telephone-based assessments in this study (43%), suggesting that the CATI method of mental health assessments may prove a better tool for the Ohio Army National Guard population.

Conclusion

The OHARNG Mental Health Initiative will continue to follow the OHARNG members over time. This longitudinal study is expected to advance the knowledge about the trajectories of post-deployment psychopathologies and facilitate enhancements in access to care and treatment of behavioral health issues among National Guard soldiers.

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Table and Figure Legends

Figure 1: 2616 Completed Surveys

Table 1: Participant Characteristics: Telephone Interview Sample Compared with Clinical Interview Subsample

Table 2: Prevalence of Mental Health Conditions for Telephone Interview Sample

Table 3: Reliability and Validity Statistics for the Telephone Assessment Sample by Psychopathology

Table 4: Sensitivity and specificity of psychopathology diagnoses by telephone within specific demographic groups

Table 4 (continued): Sensitivity and specificity of psychopathology diagnoses by telephone within specific demographic groups (continued)

Table 1: Participant Characteristics: Telephone Interview Sample Compared with Clinical Interview Subsample

Variable[a]	Telephone Interview N = 2616		Clinical Interview N = 500		P-value[b]
	n	%	n	%	
Sex					
Men	2228	85.2	440	88.0	0.10
Women	388	14.8	60	12.0	
Age, yr					
17-24[c]	878	33.6	160	32.0	0.14
25-34	848	32.5	182	36.4	
35-44	634	24.3	103	20.6	
$\geq$45	250	9.6	55	11.0	
Race					
White	2295	87.8	444	88.8	0.73
Black	195	7.5	35	7.0	
Other	123	4.7	20	4.0	
Income					
$\leq$ \$60,000	1498	59.1	279	55.8	
> \$60,001	1038	40.9	205	38.0	
Education					
High school graduate/GED or less	727	27.8	137	27.4	0.94
Some college or technical training	1234	47.2	240	48.0	
College/Graduate degree	655	25.0	123	24.6	
Marital status					
Married	1227	47.0	238	47.6	0.71
Divorced/Separated/Widowed	252	9.6	53	10.6	
Never married	1134	43.4	209	41.8	
Rank					
Officer	342	13.1	56	11.2	0.25
Enlisted/cadet/civilian employee	2273	86.9	444	88.8	
Most recent deployment location					
Never deployed	939	36.1	173	34.6	0.66
Non-conflict area	872	33.5	178	35.6	
Conflict area	793	30.5	146	29.2	
Number of lifetime deployments					
0-1	1756	67.4	323	64.6	0.49
2-3	682	26.2	143	28.6	
$\geq$ 4	169	6.5	30	6.0	
Total number of traumatic events experienced					
0	141	5.4	23	4.6	0.65
1-5	887	33.9	159	31.8	
6-11	831	31.8	166	33.2	
$\geq$12	757	28.9	152	30.4	

[a] Some percentages do not equal 100% because of missing values.
[b] chi-square tests
[c] Emancipated minors as defined by Ohio state law were eligible.

Table 2: Prevalence of Mental Health Conditions for Telephone Interview Sample

Disorder	Telephone Interview Total (N=2616)	
	n	%
Alcohol abuse [a]	628	24.0
Alcohol dependence [b]	615	23.5
Major depressive disorder [c]	270	10.3
Any depressive disorder [d]	560	21.4
Deployment-related PTSD [e,f]	121	9.6
PTSD ever in lifetime [f,g]	249	10.1
Generalized anxiety disorder [h]	45	1.7
Suicide risk[i]	49	1.9

[a] DSM-IV Criterion A (at least 1 symptom of maladaptive pattern of substance use leading to impairment or distress) and Criterion B (does not meet requirements for substance dependence ever in lifetime). Those who reported never having drunk were coded as never having the condition.

[b] DSM-IV Criterion A (at least 3 symptoms of maladaptive pattern of substance use) ever in lifetime and symptoms occurred together; MINI. Those who reported never having drunk were coded as never having the condition.

[c] DSM-IV Criteria; $\geq$ 5 out of 9 on PHQ-9, depressed mood or anhedonia, and symptoms occurred together.

[d] DSM-IV Criteria; $\geq$ 2 out of 9 on PHQ-9, depressed mood or anhedonia, and symptoms occurred together.

[e] Calculated among everyone who have deployment experience (N=1668) minus those who never experienced a deployment related traumatic event (N=374) and those who refused to answer deployment-related PTSD symptoms (N=28). Of the total sample, 9 individuals refused to say if they had ever been deployed and were coded as missing.

[f] DSM-IV Criterion A/A2 and Criteria B - F ever in lifetime.

[g] Calculated among everyone in the sample (N=2616) minus those who never experienced a traumatic event (N=141) and those who refused to answer PTSD symptoms (N=14).

[h] $\geq$ 10 on GAD-7, at least 6 months symptom duration, functional impairment, symptoms occurred together, and presence of symptoms in the past month.

[i] PHQ-9 (thoughts of wanting to hurt themselves in the past 30 days).

Table 3. Reliability and Validity Statistics for the Telephone Assessment Sample by Psychopathology

Disorder[a]	Sensitivity (SE)[a]	Specificity (SE)[b]	PPV(SE)[d]	NPV(SE)[e]	Kappa (SE)[f]	McNemar's[g]	Cronbach's alpha (standardized)[h]	AUC[i]
Deployment-related PTSD	0.50 (0.13)	0.93 (0.02)	0.35 (0.11)	0.97 (0.01)	0.36 (0.11)	1.8	0.95	0.71
Non-deployment-related PTSD	0.47 (0.13)	0.94 (0.01)	0.23 (0.08)	0.98 (0.01)	0.27 (0.09)	8.0*	0.93	0.74
Any PTSD	0.54 (0.09)	0.92 (0.01)	0.31 (0.01)	0.97 (0.01)	0.34 (0.07)	9.4*	-	-
Major depressive disorder	0.35 (0.05)	0.97 (0.01)	0.64 (0.06)	0.83 (0.02)	0.35 (0.05)	27.4*	0.66	0.77
Any depressive disorder	0.51 (0.05)	0.83 (0.02)	0.46 (0.04)	0.85 (0.02)	0.32 (0.05)	1.4	0.66	0.77
Generalized anxiety disorder	0.04 (0.04)	0.98 (0.1)	0.09 (0.09)	0.95 (0.01)	0.03 (0.05)	5.8*	0.72	0.81
Alcohol abuse	0.40 (0.04)	0.80 (0.02)	0.45 (0.04)	0.77 (0.02)	0.21 (0.04)	1.1	0.57	0.73
Alcohol dependence	0.60 (0.05)	0.81 (0.02)	0.46 (0.04)	0.88 (0.02)	0.37 (0.05)	8.5*	0.76	0.81
Suicide risk	0.32 (0.11)	0.87 (0.01)	0.55 (0.15)	0.97 (0.01)	0.38 (0.11)	3.6	-	-

[a] Criteria for telephone and clinical psychopathology assessments are explained in Table 2 footnotes.

[b] True positive/True positives + False positives with clinical interview as gold standard. SEs are asymptotic.

[c] True negatives/True negatives + False negatives with clinical interview as gold standard. SEs are asymptotic.

[d] True positive/All positives as diagnosed on the telephone. SEs are asymptotic.

[e] True negative/All negatives as diagnosed on the telephone. SEs are asymptotic.

[f] Reliability test of extent to which telephone and clinical diagnoses agree on participant classification. SE are asymptotic.

[g] Reliability test of marginal heterogeneity to see if the telephone and clinical diagnoses used different core criteria. *$P > 0.05$ suggesting differences between clinical interview as gold standard and telephone screening tool.

[h] Reliability test of internal consistency of the measurement items that make up the diagnosis

[i] Measure of overall accuracy based on the continuous score of a diagnostic test. It is the area under the ROC curve,

AUC, area under the curve; NPV, negative predictive value; PPV, positive predictive value; PTSD, post traumatic stress disorder, ROC, receiver operating characteristic; SE, standard error.

Table 4. Sensitivity and specificity of psychopathology diagnoses by telephone within specific demographic groups

Characteristics	PTSD Ever in Lifetime		Major Depressive Disorder Ever in Lifetime		Generalized Anxiety Disorder	
	Sensitivity (95% CI) [a]	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Sex						
Male	0.48 (0.28-0.67)	0.93 (0.91-0.96)	0.34 (0.24-0.43)	0.95 (0.92-0.97)	0.06 (0.0-0.29)	0.97 (0.96-0.99)
Female[a]	1 (0.29-1.00)	0.83 (0.70-0.92)	0.41 (0.18-0.67)	0.91 (0.78-0.97)	—[b]	0.98 (0.90-1.0)
Age						
17-34	0.52 (0.30-0.74)	0.93 (0.90-0.96)	0.30 (0.19-0.41)	0.95 (0.92-0.98)	—[b]	0.98 (0.96-1.0)
≥ 35	0.57 (0.18-0.90)	0.91 (0.86-0.96)	0.42 (0.28-0.58)[a]	0.92 (0.88-0.98)	0.13 (0.0-0.53)	0.97 (0.94-1.0)
Race						
White	0.55 (0.32-0.76)	0.93 (0.90-0.95)	0.34 (0.25-0.44)	0.94 (0.92-0.97)	0.05 (0.0-0.25)	0.98 (0.96-0.99)
Non-white[a]	0.50 (0.12-0.88)	0.91 (0.78-0.97)	0.38 (0.14-0.68)	0.98 (0.87-1.00)	—[b]	0.98 (0.89-1.00)

[a] Exact standard errors used to calculate 95% CI due to small sample size (< 50); otherwise asymptotic standard error used based on the fact that the outcome was rare ($P < 0.05$).

[b] n = 0 for either the telephone sample or clinical interview subsample for the specific diagnosis.

CI, confidence interval; PTSD, posttraumatic stress disorder.

Characteristics	Alcohol Abuse		Alcohol Dependence		Suicide	
	Sensitivity (95% CI)	Sensitivity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Sex						
Male	0.37 (0.28 - 0.45)	0.79 (0.74 - 0.83)	0.46 (0.37 - 0.55)	0.88 (0.85 - 0.92)	0.36 (0.13 - 0.65)	0.99 (0.98 - 1.00)
Female	0.67 (0.41 - 0.87)	0.93 (0.81 - 0.99)	0.43 (0.10 - 0.82)	0.92 (0.85 - 1.00)	0.20 (0.01 - 0.72)	0.98 (0.95 - 1.0)
Age						
17-34	0.45 (0.34 - 0.56)	0.78 (0.75 - 0.84)	0.60 (0.49 - 0.72)	0.81 (0.77 - 0.86)	0.20 (0.04 - 0.48)	0.98 (0.96 - 1.0)
≥ 35	0.40 (0.27 - 0.54)	0.75 (0.66 - 0.83)	0.59 (0.39 - 0.76)	0.83 (0.76 - 0.89)	0.75 (0.19 - 0.99)	—[a]
Race						
White	0.40 (0.31 - 0.47)	0.79 (0.75 - 0.84)	0.60 (0.49 - 0.70)	0.81 (0.77 - 0.85)	0.36 (0.13 - 0.65)	0.99 (0.98 - 1.0)
Non-white	0.50 (0.21 - 0.79)	0.86 (0.72 - 0.95)	0.60 (0.15 - 0.95)	0.90 (0.82 - 0.98)	0.20 (0.01 - 0.72)	0.96 (0.86 - 1.0)

[a]n = 0 for either the telephone sample or in-person clinical interview subsample for the specific diagnosis.

CI, confidence interval.

CONTINUING REVIEW ABSTRACT & STATUS REPORT

TITLE: Ohio Army National Guard Mental Health Initiative (OHARNG MHI): Risk and Resilience Factors for Combat-Related Posttraumatic Psychopathology and Post Combat Adjustment

IRB#: 03-06-46

ABSTRACT

SUMMARY OF PURPOSE, AIMS, & OBJECTIVES:
Since 2005 a team of investigators have been working with Congresswoman Marcy Kaptur and the Department of Defense on operationalizing the Ohio Army National Guard Mental Health Initiative (ONARNG MHI). The general objective of this effort is to evaluate the relationships between risk and resilience factors, both cross-sectionally and longitudinally, before, during, and after deployment.

The primary research project for this initiative was garnered through a 2006 Department of Defense congressional special interest award and is entitled "Risk and Resilience Factors for Combat-Related Posttraumatic Psychopathology and Post Combat Adjustment". The protocol and study documents were reviewed by the U.S. Army Medical Research and Materiel Command (USAMRMC), Office of Research Protections (ORP), Human Research Protection Office (HRPO) and found to comply with applicable DOD, U.S. Army, and USAMRMC human subjects protection requirements on October 1, 2008.

The Coordinating Principal Investigator for the project is Joseph R. Calabrese, MD, and the Co-Principal Investigator, Marijo Tamburrino, MD (University of Toledo). Field Procedures are directed by Sandro Galea, MD, Dr.PH, Professor of Epidemiology and Chairman, Mailman School of Public Health, Columbia University. Responsible for the development of future Translational Research projects will be Israel Liberzon, MD, PhD, Professor of Psychiatry & Neuroscience, Ann Arbor VA. The Coordinating Center is based out of University Hospitals Case Medical Center at Case Western Reserve University. The survey firm, Abt SRBI, Inc., carries out telephone interviews and investigators at University Hospitals Case Medical Center and the University of Toledo carry out in-person research assessments. The data is stored at Abt SRBI, Inc. for the Telephone Survey and psychosocial data associated with the Genetics Study. The In-Person Survey data is stored at Michigan State University's Biomedical Research Informatics Core headed by Philip Reed, PhD. DNA saliva samples are stored at the Ann Arbor VA.

This initiative is overseen by the Ohio National Guard, the Office of Congresswoman Marcy Kaptur, the Department of Defense's Military Operational Medicine Research Program (MOMRP) and the Telemedicine & Advanced Technologies Research Center (TATRC) (last annual Product Line Review Meeting on February 19, 2013), the Initiative's External Scientific Advisory Board (last annual meeting April 2, 2012) and External Administrative Advisory Board (last annual meeting May 16, 2012).

The primary study within this initiative is a clinical epidemiology and health services project and is designed to function as the template, upon which other projects, including but not limited to those of a translational research nature, will be added. Accordingly, this project has obtained permission to re-contact previously studied, well-characterized research subjects and their family members for future research that specifically targets the

improvement of the scientific understanding of combat-related posttraumatic psychopathology and similar adjustment problems.

METHODOLOGY:
This project is designed to interview a representative sample of at least 3,000 members of the Ohio National Guard on an annual basis for 10 years, which started in November 2008. These Guard members participate in the primary sample and complete an interview over the telephone. Group assignment to the telephone interview is made randomly from the entire population of the Ohio National Guard (~12,000) on an ongoing basis with the dynamic cohort sampling each year of new members of the Ohio National Guard. In addition, 500 participants, randomly selected at baseline from the telephone sample, complete annual in-person interviews as a part of a validation sub-sample. The dynamic cohort implemented in 2010 also refreshes the sample size due to lost to follow ups, deployments, etc. We have obtained a random representative sample of National Guard members that will have variable lengths of involvement and combat exposures, allowing us to adequately address the proposed aims.

The Telephone Survey requires 60 minutes on average (depending on the individual history of the service member) and constitutes the primary dataset, whereas the In-Person Survey requires 2-3 hours (depending on individual history). The In-Person Survey is used to validate key domains employed in the telephone survey, gather more in-depth information and across different domains, and to further study of the longitudinal trajectory of PTSD. The Genetics Repository began in May 2010 and all cohort participants from the main study are being approached to provide informed consent, complete a self-report survey, and provide a saliva sample from which DNA will be extracted.

During Project Year 5 (November 2012 through 2013), data collection will be put on hold for the Telephone and In-Person Surveys. Year 4 interviews were completed through December 2012 as previously planned.   In 2013, the investigators will focus on additional data analyses, publications, and dispersal of the study results (task 3 of the scope of work) with the remaining funds. Data collection will resume when additional grant funding is obtained, which the investigators are continuing to actively pursue.

STATUS REPORT

Summary
Over the past year, the OHARNG MHI has finished collecting data for Year 4 of the main project and has continued to work on task 3 of the scope of work (data analyses, publications, etc.). Year 4 began on November 17, 2011 for the Telephone Survey and December 12, 2011 for the In-Person Survey.

Telephone Survey (interviewed by Abt SRBI, Inc):

Year 4 Interviews:
Year 4 in the Telephone Survey began November 17, 2011 with 11 pilot interviews. The Y4 Telephone Survey was deemed to be an average of 41 minutes for participants who have not been deployed in the past year, and 58 for participants deployed within the past year (since their last interview). Since the average duration is within 1 hour which is the maximum stated in the protocol and verbal consent script, cuts to the survey content did not need to be made.

Data collection for Year 4 and the Dynamic Cohort ended on 1/31/2013. A summary of enrollment activity since the last CR is as follows:

- 1,428 out of 2,616 Year 4 interviews have been completed thus far. The cooperation rate for Year 4 Telephone Survey is 81.8%. The participants who declined did not withdraw from the study but were not able to complete the Year 4 survey at the time they were contacted. They will be recontaced if/when data collection resumes.

Dynamic Cohort Year 4 Telephone Survey Interviews:
A summary of enrollment activity since the last CR is as follows:

- N=263 DC-B interviews have been completed thus far. The cooperation rate for the DC-B survey is 54%.

Telephone Survey Withdrawals:
No participants from the main survey were withdrawn by the PI. One participant disenrolled from the study due to death since September 17, 2012 (when this was reported in last year's continuing review). Three participants withdrew from the study voluntarily.

Since the beginning of the main telephone survey, 45 participants have withdrawn from the main survey voluntarily and 10 disenrolled from the study due to death. Please see Appendix A for a report from the telephone survey firm, Abt. SRBI.

Telephone Survey Cumulative Enrollment and Interview Summary:

Project Year	Actual Enrollment	Projected Enrollment	Total Enrollment	Interviews Completd
Year 1 2008-2009	2,616	0	2,616	2,616
Year 2 2009-2010	0	0	0	1,770
Year 3 2010-2011	578	0	578	1,973
Year 4 2011-2012	263	0	243	1,691
Year 5 2012-2013*	0	0	0	
Year 6 2013-2014**		450	450	
Year 7 2014-2015		450	450	
Year 8 2015-2016		450	450	
Year 9 2016-2017		450	450	
Year 10 2018-2019		450	450	
Total	**3,457**	**2,250**	**5,707**	**8,050**

*Year 5 data collection hiatus - see protocol
**Assumptions - 15% will be lost to attrition (deployment, lost to follow-up, declined,etc) of 3,000 interviews being completed

Genetics Study (approached by Abt SRBI, Inc. interviewer at the end of the Telephone Survey):
Recruitment began on May 3, 2010. A summary of enrollment activity is as follows:
1. N=2,720 participants (N= 142 since the last CR) have been approached on the Telephone Survey (Year 2, Year 3, Dynamic Cohort Baseline, Year 4 Dynamic Cohort).
2. N=2,049 participants (N= 97 since the last CR) have agreed to receive the Genetics Kit via mail (75% positive response)
3. N=1,104 participants (N= 29 since the last CR) completed kits (consent form, self report survey, and saliva DNA sample) have been returned (53% return rate).

In-Person Survey (interviewed by UHCMC and UT clinician interviewers):

Year 4 Interviews
Year 4 pilot interviews began on December 12, 2011 and ended on January 31, 2012. A total of N=20 interviews were completed. As the average time to complete the Clinician Rated Survey was 2 hours, and the Self Report Survey was less than one hour, the overall durations of 2-3 hours was achieved. No major cuts besides administrative updates; i.e. skip patterns, page numbers, etc. needed to be done. A summary of enrollment activity is as follows:
1. Year 4 Interviews Completed: N=436 out of 500. UHCMC site N=250; UT site N=186
2. Year 4 Declined participants : N=8
3. Year 4 Delayed participants: N=3
4. Year 4 Lost to follow-up participants: N=63
5. Year 4 Deployed participants: N=13

Dynamic Cohort Baseline
Year 4 Dynamic Cohort pilot interviews began on February 27, 2012. As the average time to complete the Clinician Rated Survey was 2 hours, and the Self Report Survey was less than one hour, the overall durations of 2-3 hours was achieved. No major cuts besides

administrative updates; i.e. skip patterns, page numbers, etc. needed to be done. A summary of enrollment activity is as follows:

1. Dynamic Cohort Interviews Completed: N= 67, UHCMC site N=50; UT site N=17;
2. Screen Failures N=32 (4 since the last CR) for the following reasons: unable to contact, not interested, and too busy

In-Person Survey Cumulative Enrollment and Interview Summary:

Project Year	Actual Enrollment	In-Person Survey Enrollment		Interviews Completed
		Projected Enrollment	Total Enrollment	
Year 1 2008-2009	500	0	500	500
Year 2 2009-2010	0	0	0	418
Year 3 2010-2011	105	0	105	461
Year 4 2011-2012	67	0	67	503
Year 5 2012-2013*	0	0	0	0
Year 6 2013-2014**		0	0	0
Year 7 2014-2015		0	0	0
Year 8 2015-2016		0	0	0
Year 9 2016-2017		0	0	0
Year 10 2018-2019		0	0	0
Total	672	0	**672**	**1,882**

*Year 5 data collection hiatus - see protocol
**In-Person survey will not continue after Project Year 5 due to limited funds

In-Person Survey Withdrawals:
Since the beginning of the In-Person Survey, a total of 54 participants have withdrawn from the study, 3 since the last continuing review. Participants withdraw for the following reasons: no longer interested in participating, too busy, and unable to contact two consecutive years (PI withdrawn).

Adult Relative Registry (approached by the In-Person team):
Recruitment into the Registry remains closed. When an ancillary family study is funded the investigators will inform the IRB and will re-open recruitment if needed.

Total Summary Enrollment Table:

Telephone Survey and In-Person Survey Summary Table				
Project Year	Actual Enrollment	Projected Enrollment	Total Enrollment	Interviews Completed
Year 1 2008-2009	3,116	0	3,116	3,116
Year 2 2009-2010	0	0	0	2,188
Year 3 2010-2011	683	0	683	2,434
Year 4 2011-2012	330	0	330	2,194
Year 5 2012-2013*		0	0	
Year 6 2013-2014**		450	450	
Year 7 2014-2015		450	450	
Year 8 2015-2016		450	450	
Year 9 2016-2017		450	450	
Year 10 2018-2019		450	450	
Total	4,129	2,250	6,379	9,932

EVENT REPORTING: ADVERSE EVENTS, UNANTICIPATED EVENTS, AND PROTOCOL DEVIATIONS

Serious Adverse Events

There has been 0 Serious Adverse Event since the last CR report.

Unanticipated Problems

There has been 1 unanticipated problem over the past year since the last CR report.

1. October 2012: Two participants who were already enrolled in the main cohort were also enrolled and completed an interview for the Year 4 Dynamic Cohort. Both participants were paid but will not be included in the final dataset for the Year 4 Dynamic Cohort and will remain in the main cohort dataset. One of the two participants was sent to the Coordinating Center as they had expressed interest in the in-person survey. Participant 4040 was not previously contacted to enroll in the in-person survey. They completed the in-person survey on 3/29/2012 and will remain in the Dynamic Cohort Year 4 cohort.

Protocol Deviations

Over the past year since the last CR, there have been 2 protocol deviations reported to the IRB and DSMB:

1. November 2012: On November 16, 2012 the Coordinating Center discovered a problem with 1 optional audio consent forms for the In-Person Survey. During the Quality Assurance process it was discovered that one interviewer used an expired, outdated version of the optional audio consent form with participant 0927 during their Year 4 interview on 10/3/2012. On August 21, 2012, an updated audio consent form was approved adding text to allow the audio files be shared with researchers

interested in collecting and analyzing de-identified data. Participant #0927 signed the 11/24/2010 version.

2. April 2013: Participant 3028 completed his Year 4 in-person interview on November 13, 2012. While cleaning up the data for Year 4 on April 25, 2013, the Coordinating Center caught that the informed consent signed by this participant was expired at the time the interview was conducted. This deviation was missed during the quality assurance process. The participant was contacted to sign a new consent form so his data could be used. To date, the participant has not yet returned the updated signed consent form so his data has remained quarantined.

The following minor deviations occurred over the past year since the last CR and per IRB event reporting policy are kept in the investigator's file: See Appendix B for the detailed memo to file reports of the below minor deviations.

1. November 2012 – Participant #0110 signed an informed consent form that had different version dates.
2. February 2013 – Over N=500 participants were enrolled in the in-person survey, but not significant enough to be considered a major deviation
3. May 2013 – Participant 0624 printed his/her name on the informed consent but did not sign it as required
4. May 2013 – Participant 3185 incorrectly dated the main and audio informed consent

SUBJECT COMPLAINTS:

On June 13, 2013 a telephone survey participant's mother sent the following email to PI, Dr. Joseph Calabrese, after receiving the project's IRB approved Spring 2013 newsletter:

Dr. Calabrese,

I am the mother and NMA of SPC (participant's name) who is part of your ONG study. We received the Spring 2013 flyer this week and I wanted to share from the perspective of a mother/family member, living with a soldier with PTSD and depression.

I do agree with your statement in the 'General Take Home Message' that there are vulnerable subgroups who are more prone to these conditions. However, I don't feel any kind of specialized training at enlistment can prepare these soldiers for the after-math of war. Most of these men and women are young when they enlist, most right out of high school. Any training of this type will be forgotten by the time something of this magnitude occurs. My son was a fine soldier until he was critically injured in Afghanistan in 2012. As a parent, living through it daily, there was nothing that could have prepared my son for what he has experienced, nor what he lives with every day of his life now. It is my opinion, constant follow up and treatment after the fact, is the best for these soldiers, again, in my opinion, there is nothing that can prepare anyone for this. Along with that, none of these soldiers think it will ever be them so would they really gain anything at enlistment?

I would like to add, I am very discouraged that no one from the OHARNG has made any contact regarding my son. To me, this certainly doesn't show any kind of concern for what you're trying to accomplish in your study. I must say, it's perplexing.

With all of this being said, I would be happy at any time, to converse with you or any of your team regarding living with a soldier with PTSD and depression. This is our new norm in which we are all trying to adjust to.

In follow up to this email Dr. Calabrese scheduled a teleconference with the participant's mother. During the call, this woman explained to Dr. Calabrese her understanding of her son's illness. Dr. Calabrese then took the time to explain the illness to the participant's mother. The call lasted for 45 minutes and the mother was extremely appreciative that Dr. Calabrese took the time to follow up with her.

.**RECRUITMENT/RETENTION PROBLEMS**
N/A due to data collection hiatus

STUDY FINDINGS
Please find attached a **Progress Report** Appendix C, detailing the Year 4 completed interviews demographic information and abstracts of recently analyzed results (not yet published).

3 manuscripts have been published or accepted for publication since the last continuing review; 10 total manuscripts have been publised – See Appendix D for recently accepted publications:
1. Prescott, M. The Ohio Army National Guard Mental Health Initiative: Data Collection, Sampling, Validation and Baseline Results. International Journal of Methods in Psychiatric Research, *in press.*
2. Goodwin, R. Smoking is a predictor of depression onset among National Guard soldiers. Psychiatry Res 2013 Apr 30;206(2-3):321-3. PMID:23291043
3. Fine, T. Validation of telephone-administered PHQ-9 against the in-person administered SCID-I major depression module. J Affect Disord. 2013 June 6, Epub ahead of print]. PMID: 23747208

RISK/BENEFIT RATIO

The risk/benefit ratio remains unchanged for this mild-risk, non-interventional study. There have not been any relevant publications or data that the investigators are aware of that would affect the risk/benefit ratio of the study.

DATA SAFETY & MONITORING BOARD

Since the last CR, the independent DSMB met on February 12, 2012 and November 12, 2012, and the next meeting is slated for August 29, 2013. Please see attached letters allowing the study to continue that were submitted to the IRB on File during the year. The DSMB members did not have any recommendations for the study team or reservations about the study proceeding as planned. If any SAEs should occur over the next year, the DSMB Chair, Dr Seagraves, will review in real time. Due to the data collection hiatus, the DSMB will only meet twice in 2013. We do not foresee any SAEs occurring during this time period or any other events that would need the attention of the DSMB members.

TRIAL REPORTS FROM MULTI-CENTER SITES

n/a

CONFLICT OF INTEREST

n/a: There has not been a change in investigator conflict of interest over the past year.

ADDENDA APPROVED OVER THE PAST YEAR:

The following addendum submissions were submitted and approved by the IRB during the past year covered by this review. Please note that only major submissions including an "Amendment" document, numbered sequentially, and are noted below as applicable. The submissions included the following documents:

1. November 2012: The project added two students to the protocol -Yiying (Elaine) Liu and Srijita Sarkar
2. May 2013: The Spring 2013 Newsletter was IRB approved on May 9, 2013 and sent to all participants shortly after.
3. August 2013: A protocol addendum was IRB approved on August 15, 2013 to re-consent subjects in the in-person survey so their audio files can be used for additional research, specifically with Intelligent Automation Inc.

PLAN FOR UPCOMING YEAR:

Please see attached most recent quarterly report to TATRC/USAMRMC Appendix E (submitted July 12 2013) which also details upcoming plans for the project.

I. **No-cost extension request submitted on July 9, 2013:** The Coordinating Center is estimating that $200K will remain in award W81XWH-10-1-0579 when the contract ends on 9/27/2013. To spend the remaining funds, Dr Calabrese has submitted a no-cost extension request to continue prioritizing the work performed on Task 3 and Task 4, as well as to keep the existing infrastructure intact for the next generation of the project, which will includes the submission to the Joint Warfighter Medical Research Program further outlined in later text. The below text outlines the no cost extension request in more detail:

   a. **Scope of Work Task 3**: "Performance of a descriptive analysis of the data collected from the primary and sub-sample group. At least one peer-reviewed publication per year will be derived"

As previously stated, this no-cost extension will allow the investigators additional time and resources to devote to Task #3 of the Scope of Work. There are currently 14 manuscripts in process that will be submitted to scientific journals (to be determined) over the next 6 months – please see manuscripts and corresponding authors listed below.

1. War and civilian-related PTSD (Prescott)
2. Childhood experiences are a determinant of depression in adulthood (Rudenstine)
3. Ethics in trauma research (Fine)
4. Pre/peri/post supports and their associations with alcohol abuse (Orr)
5. Non-medical prescription drug use is a major public health problem among veterans returning from areas of conflict (Cerda)
6. Deployment-related sexual harassment at T1 (Walsh)
7. PTSD factors related to risky driving and substance abuse (Elhai)
8. Demographic variables moderate the relationship between PTSD and emotional regulation (Elhai)
9. PTSD factors that best predict/drive the other PTSD factors over 3 years (Elhai)
10. SNPs in the "PACAP receptor" gene (ADCYAP1R1) association with PTSD severity in males and females (Liberzon)
11. Posttraumatic stress disorder (PTSD) and alcohol use disorders (AUDs) at T1, T2, and T3 (Walsh)
12. Prevalence and Determinants of mild TBI in the Ohio National Guard (Sampson)
13. Longitudinal trajectories of 12-month PTSD and depression in the Ohio National Guard (Sampson)
14. Type and setting of potentially traumatic events as determinants of 12-month depression in the Ohio National Guard (Sampson)

Dr. Sandro Galea and his team of analysts are working closely with the leadership of the Ohio National Guard to obtain full demographics of the Ohio Army National Guard when the project first started in 2008. The demographics will include gender, age, race, rank, marital status, deployment, total days mobilized, ethnicity, and civilian education. This information will ensure sure that analyses going forward will best represent the entire OANG population, not just our sample. In other words, it will be used for constructing population weights, a behind the scenes process that is very important for conducting analyses, and then drawing appropriate conclusions about those findings.

In addition, the Coordinating Center has recently hired a new data analyst, David Fink MPH, whose sole responsibility will be to prepare data and perform statistical analyses on data collected relating to the OHARNG MHI clinical sub-sample dataset. These meaningful and scientifically compelling analyses will be turned into manuscripts which will be submitted to accredited journals approved by the Steering Committee. David will be expected to publish 2-3 manuscripts over the next 12 months.

David has experience as an epidemiologist with the United States Army Institute of Public Health where he contributed to the design and execution of epidemiological surveillance, analytical projects and behavioral and social health investigations such as suicide, domestic violence, child abuse and homicide rates. David also has experience with the VA in San Diego where he was the Research Manager of three components of a large integrated prospective study of active duty Marines pre and post deployment.

b. **Scope of Work Task 4**: "Annual oversight meetings for the Initiative, including the External Scientific Advisory Board and the Administrative Advisory Board"

Scientific Advisory Board
The no-cost extension will also be used to fund the annual Scientific Advisory Board (SAB) meeting, scheduled for October 16th, and Administrative Advisory Board meeting, scheduled for October 17th. The SAB is comprised of nationally and internationally renowned individuals with established scientific credibility, and a strong record of scientific productivity and scholarship. This year we are happy to announce two new members of our SAB, COL Carl Castro, PhD, Director MOMRP and Dr. Dan Kivlahan, PhD, Director Center of Excellence in Substance Abuse Treatment and Education. This year we have two new members, including COL Castro, PhD, Director MOMRP and Dr. Dan Kivlahan, PhD, Director Center of Excellence in Substance Abuse Treatment and Education. COL Castro has published over 60 scientific articles in the area of PTSD, mental health training, and mTBI and Dr. Kivlahan has published over 100 with a scientific focus on substance abuse disorders and co-occuring conditions, including PTSD. Both are thought and established scientific leaders who will provide the investigators with unbiased critical feedback on the scientific merit on the continuation and expansion of the project.

The agenda for this years SAB meeting will primarily focus on the next generation of the project, including the primary platform, the secondary platform, and the alcohol prevention and intervention project.

Administrative Advisory Board
The Administrative Advisory Board meeting includes state and local leaders, administrators, and stakeholders, and provide guidance on non-scientific issues. The attendees include 1) The Adjutant General Deborah Ashenhurst 2) Col. John Harris (Ohio National Guard Deputy Chief of Staff of Personnel), and 3) US House of Representative Congresswoman Marcy Kaptur (District 9) or her representative. This meeting provides substantive feedback to the investigators on how the study data is relevant to the Ohio Guard population. Since 2008, the Guard has been actively involved in project development. The leadership of the Ohio Guard was extremely supportive during the development and submission of the alcohol intervention project submitted to the BAA on 2/1/13 (discussed further below). Based on results from the OHARNG MHI sample, the alcohol project was conceptualized at the 2012 AAB meeting. The ONG leadership was fully supportive and invested in the funding of this project. If funded and successful, the Guard is hopeful to use this intervention tool that all Guard members can use.

In addition, the leadership of the ONG will be intimately involved in the start up of a secondary platform. The leadership has expressed their willingness to assist us in the expansion, which may include engaging the National Guard Bureau and the second state's Guard leadership. The agenda this year will focus on the implementation of the alcohol project, if funded, and the next generation of the OHARNG MHI.

Congresswoman Kaptur
Each year Dr. Calabrese and Dr. Tamburrino meet with Congresswoman Kaptur to give her an update on the progress of the initiative. The meeting this year with will be held in late spring or early fall in Washington DC. Most recently, Congresswoman Kaptur spoke on behalf of Dr. Calabrese and the OHARNG MHI in the House of Representatives applauding his efforts on the project. "…because Doctor Calabrese has taken the lead role in a major initiative that I helped launch under the auspices of the U.S. Department of Defense to study the effects of post-traumatic stress disorder on soldiers returning from combat zones. I have watched as Doctor Calabrese, working in concert with doctors at the University of Toledo, has conducted truly groundbreaking research involving combat veterans who suffer from PTSD. I have long been concerned about the incidence of suicide among our combat veterans. In communities and families throughout our country, we have seen the devastating impact of PTSD. The ambitious research project by Doctor Calabrese that I have been privileged to support has studied the relationship between PTSD and suicidal ideation among members of the Ohio Army National Guard". The meeting this year will focus on the next generation of the project and Congresswoman Kaptur's vision for the continuation and expansion of the initiative.

II. **Alcohol prevention and intervention:** The alcohol project under the leadership of Dr. Fred Blow and Dr. Calabrese submitted to the BAA on February 4th has positively passed scientific peer review and is pending programmatic review to determine the level of funding. If the alcohol project is funded, the OHARNG MHI infrastructure will provide support through a project manager, research assistant, and data coordinator during study start up (anticipated start date 8/1/2013), recruitment (anticipated start date 1/1/2014), and project implementation (anticipated start date 7/1/2014). In addition, Dr. Calabrese and Dr. Blow will be intimately involved with the leadership of the Ohio Guard in creating and implementing the alcohol intervention computer assisted program.

III. **Joint Warfighters Research Program Application**: Most recently, the investigators submitted an application asked to submit an application to the Joint Warfighters Research Program Application. This application was submitted on July 26th and, if approved, will fund Wave 5 data collection of the primary platform (telephone survey). The investigators are expected to hear of funding by October 2013 and data collection would begin on 1/1/2014.

IV. **Broad Agency Announcement FY15**: In the next few months, the investigators plan on submitting a pre-proposal to the Broad Agency Announcement to continue data collection for Waves 6-10 for the primary platform. The Joint Warfighters application

mentioned above is intended to fund Wave 5 and the BAA is intended to fund Waves 6-10.

V. **Michigan State University**: On September 27, 2013 UHCMC's subcontract with The Biomedical Research and Informatics Center (BRIC) at Michigan State University (MSU) will come to an end. MSU provided clinical research informatics support for the in-person survey portion of this project and was led by Investigator Philip L. Reed, PhD, MSc. Until further notified, the in-person survey will no longer continue collecting data due to funding. However, the data collected through Wave 4 will continue to be analyzed in order to produce manuscripts which will be submitted to scientific peer reviewed journals.

The in-person data that has been housed at MSU will remain on MSU's servers in hot storage. Hot storage allows the database to remain active to allow for additional manipulation of the data after ending study data collection. The fees that were paid to maintain the database on May 7, 2013 allows the study database to be active until May 6, 2014. In addition, MSU grants an additional year of grace period, free of charge, in case a study becomes active once again. Therefore, the database will remain active until May 2015.

The project will continue sharing data among the various sites through Sharepoint offered by MSU, unless a local institutional copy of Sharepoint is available. If a local copy of Sharepoint is available, all data contained on MSU's Sharepoint account will be exported to University Hospitals' servers (or within the local CTSC) and then stored onto the local institutions copy of Sharepoint. The Coordinating Center will work with the legal department/pre-award office to ensure that an agreement is in place to continue using Sharepoint through MSU's servers.

University Hospitals
Case Medical Center

IRB APPROVAL NOTIFICATION

The University Hospitals Institutional Review Board (IRB) has reviewed the following submission:

Principal Investigator: Joseph R Calabrese
Protocol Title: Risk and Resilience Factors for Combat-Related Posttraumatic Psychopathology and Post Combat Adjustment
UHCMC IRB number: 03-06-46

Submission Type: UH IRB Continuing Review

Review Type: Full Board

Date of Committee Review: 09/03/2013

As such, the UHCMC IRB has determined that with respect to the rights and welfare of the individuals, the appropriateness of the methods used to obtain informed consent and the risks and potential medical benefits of the investigation, the current submission is acceptable under Federal Human Subject Protection regulations promulgated under 45 CFR 46 and 21 CFR 50 and 56.

Date of Approval: 09/03/2013

The current expiration date for this study is: 09/02/2014
(The expiration date is the last day that a protocol has IRB approval)

- Per Federal regulation, changes MAY NOT be made to any element of the current research without prior IRB approval, except to eliminate an immediate and apparent hazard to subjects enrolled in the trial.

- Per Federal regulation, the research may not continue without IRB approval. You must submit a request for continuation at least 6-8 weeks prior to the expiration date noted above.   Once the study is complete, the IRB requires prompt notification of study closure.

- Failure to retain current IRB approval may result in archiving of the current study and human subjects non-compliance allegations.

Documents reviewed and/or approved as part of this submission:

Title	Version Number	Version Date
RR Project - CR status report v8-21-2013	Version 1.0	08/21/2013
UHCMC CR report FINAL 8.12.13	Version 1.0	08/12/2013
signed dod dsmb memo 11-12-2012	Version 1.0	11/01/2012
signed dod dsmb memo	Version 1.0	02/01/2013

Human Risk: [Risk for adults] Not Greater Than Minimal Risk

Vulnerable populations approved for inclusion: Pregnant Women (being recruited for study participation)

p. 1 of 2 for Joseph R Calabrese iRIS Reference # 027711

Funding Source: Department of Defense

Other information: Waiver of HIPAA Authorization and Waiver of Signed Consent (45 CFR 46.117(c)(2) for Telephone Survey, In-Person Survey, Adult Relative Registry

Approval Signature:

UHCMC IRB Chairperson
(Signature was applied by the IRB Administration Office)

The UHCMC IRB operates under the HHS Federal Wide Assurance of Compliance number 00003937 and IRB registration numbers 00000684, 00001691 and 00008600

p. 2 of 2 for Joseph R Calabrese iRIS Reference # 027711

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Ohio Army National Guard Mental Health Initiative

Coordinating PI: Joseph R. Calabrese, MD

Award Number (s):   W81XWH-07-1-0409: 5/7/2007 – 5/6/2012

W81XWH-10-1-0579: 9/28/2010 – 9/27/2013

Award Amount: $12.308 million

Contract Officer: Amber Shryer

Project Officer: Ruchi Malik

University Hospitals
Case Medical Center

SCHOOL OF MEDICINE
CASE WESTERN RESERVE
UNIVERSITY

Co-PIs & Acknowledgements

Columbia University
Scientific Principal Investigator – Sandro Galea, MD, DrPH

Ann Arbor VA
Dir., Translational Research - Israel Liberzon, MD

University of Toledo (UT)
Co-PI – Marijo Tamburrino, MD

Michigan State University
Co-Investigator Director of Informatics - Philip Reed, PhD, MS

Abt. SRBI, Inc
Telephone Survey Data Collection Firm – Mark Morgan

Ohio National Guard

TAG Deborah Ashenhurst   Jeremy Kauffman, Psy   Colonel Julie Blike
ATAG John Harris   Captain Sephan Frazier

Background & Rationale

Existing Efforts

- **1st prospective study to use pre- and peri- deployment Guard data to meet the real-time prioritized translational needs of vulnerable subgroups.**
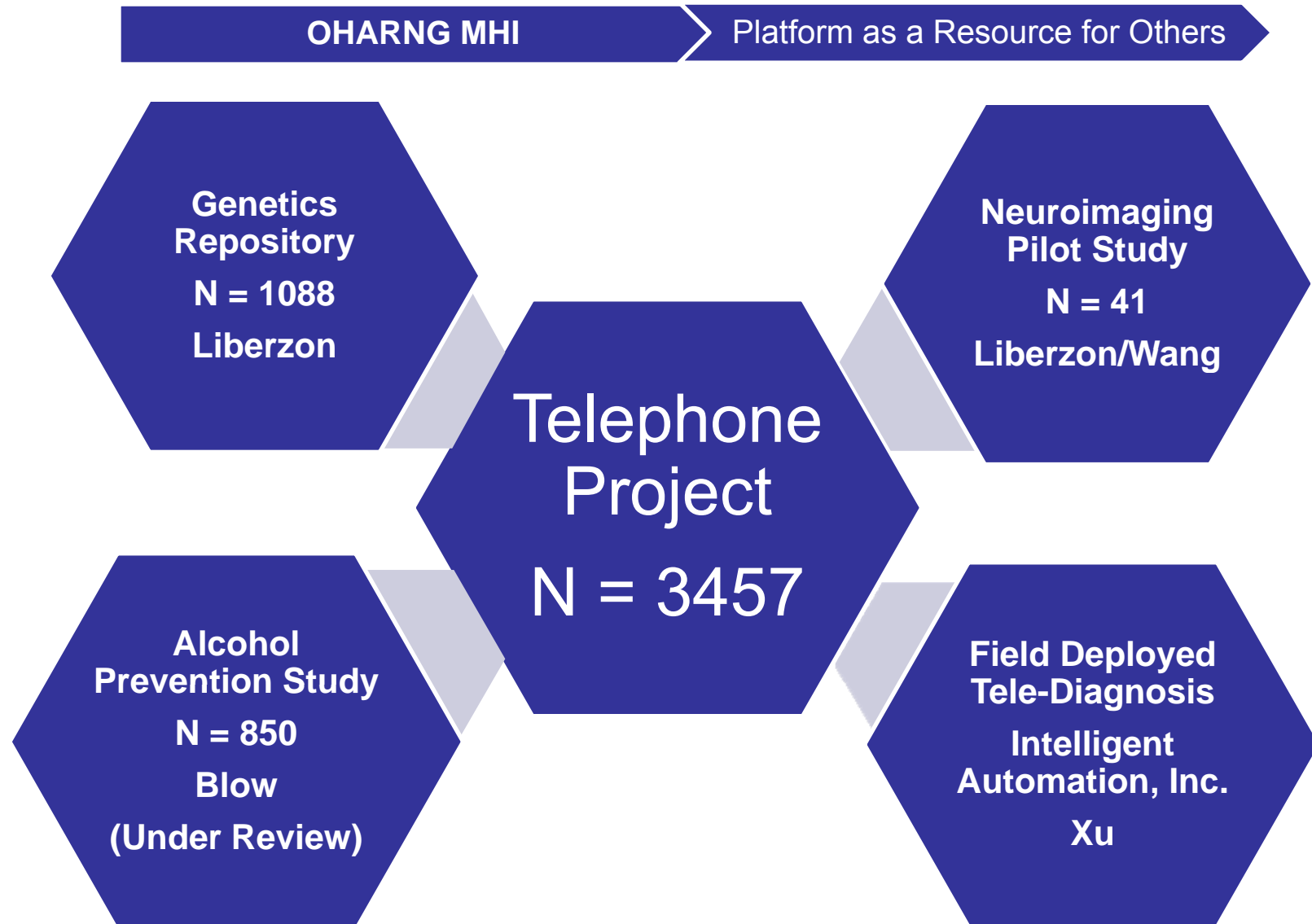
Uniqueness

- **A focus on how pre-, peri-, and post-deployment factors jointly predict distinct trajectories of posttraumatic psychopathology**
- **A focus on how interpersonal, intrapersonal, and contextual factors jointly predict distinct trajectories of posttraumatic psychopathology**
- **A focus on how both military and civilian experiences shape longitudinal risk for psychopathology.**
- **1st study to generate an association with PTSD symptoms in soldiers deployed to Iraq and Afghanistan, while replicating previous findings of G x E interaction effects in FKBP5 and 5-HTTLPR (ACNP 2012)**

Value

- **Feedback from leadership led to a 2013 submission targeting the development of a secondary prevention study targeting hazardous alcohol use in soldiers not yet deployed (Fred Blow-currently under review)**
- **Study results let to revisions of the Ohio Guard's Suicide Prevention Annual Training using In Press data that highlighted the relationship between suicide and Axis I comorbidity (Calabrese et al 2011)**

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Study Value

OHARNG MHI | Platform as a Resource for Others

Genetics Repository

N = 1088

Liberzon

Neuroimaging Pilot Study

N = 41

Liberzon/Wang

Telephone Project

N = 3457

Alcohol Prevention Study

N = 850

Blow

(Under Review)

Field Deployed Tele-Diagnosis

Intelligent Automation, Inc.

Xu

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Research Questions & Hypotheses

Telephone Project

- **AIM 1: Examine the roles of pre-, peri, and post-deployment experiences, both military and civilian, in jointly contributing to tristories of psychopathology over a decade of follow-up.**
  - H1 - Pre-, Peri-, and post-deployment factors will jointly predict distinct trajectories of posttraumatic psychopathology.
  - H2 - Interpersonal, intrapersonal, and contextual factors will jointly predict distinct trajectories of posttraumatic psychopathology.
  - H3 - Military and civilian experiences co-equally shape longitudinal risk for psychopathology among ONG soldiers.
- **AIM 2: To assess the polygenic drivers of the trajectories of psychopathology over long-term follow-up of a reserve population.**
  - H1 - Trajectories of psychopathology over a decade of follow-up will be predicted by genetic markers at multiple loci.
  - H2 - Genetic loci will act in concert with environmental factors (e.g. traumatic events, social support, and geographic features) to shape trajectories of psychopathology.
- **AIM 3: To examine the role of hazardous alcohol use and alcohol use disorders in the multimorbidity of PTSD, depression, TBI and other psychopathology, and their chronicity over a decade of follow-up.**
  - H1 - Hazardous alcohol use and alcohol use disorders will be associated with new onset of psychiatric disorders.
  - H2 - Hazardous alcohol use and alcohol use disorders will strongly predict chronicity of comorbid psychiatric disorders.

Genetics Repository

- **AIM 1:** Identify specific molecular genetic factors associated with vulnerability and resilience to deployment- and combat-related psychiatric disorders
  - **H1 –** Genetic variants are associated with post-deployment PTSD and other stress-related psychiatric syndromes and symptoms in military personnel.
  - **H2 –** Risk alleles interact with the severity and characteristics of deployment stress (e.g. combat, accident), and with pre- and post-deployment environmental factors (e.g. psychosocial factors including lifetime stress / trauma history, early life adverse events) to lead to greater PTSD risk following trauma.

Neuroimaging

- **AIM 1:** Demonstrate differential activation patterns in response to: emotional processing tasks, cortical thickness of activated regions, and white matter connectivity of frontal cortex and amygdala in adults with a history of childhood adversity (CA) who develop PTSD, adults with CA who developed PTSD after adulthood deployment-related trauma, and adults with both CA and adult trauma who did not develop PTSD
  - **H1 –** Childhood adversity shapes neurocircuits underlying emotional regulation, which can lead to PTSD development after CA or upon exposure to additional trauma in vulnerable individuals, but not in highly resilient individuals
- **AIM 2:** Explore the feasibility of gene (stress-related) by environment (CA) interactions on promoting changes in brain function (amygdala and mPFC response to emotion tasks) and structure (cortical thickness and white matter connectivity) known to be associated with PTSD after child and/or adulthood traumas.
  - **H2 –** Childhood adversity interacts with genetic factors to produce individual differences in brain structure and function, which contribute to vulnerability/resilience to the development of PTSD upon adult trauma exposure

Intelligent Automation, Inc.

- **AIM 1**: Use of an automated Tele-PTSD monitoring system to assist in the diagnosis of PTSD.
  - **H1 –** Voice patterns of PTSD patients will differ from healthy controls

Alcohol Intervention

- **AIM 1**: Compare web- and text-based alcohol brief interventions (WT-BI) and Enhanced Usual Care (EUC).
  - **H1 –** Participants randomized to the WT-BI condition will report significantly fewer days/weeks drinking and fewer drinks/day than participants in the EUC condition at follow-ups
  - **H2 –** Participants randomized to the WT-BI condition will report significantly fewer binge drinking episodes compared to the EUC participants at follow-ups.
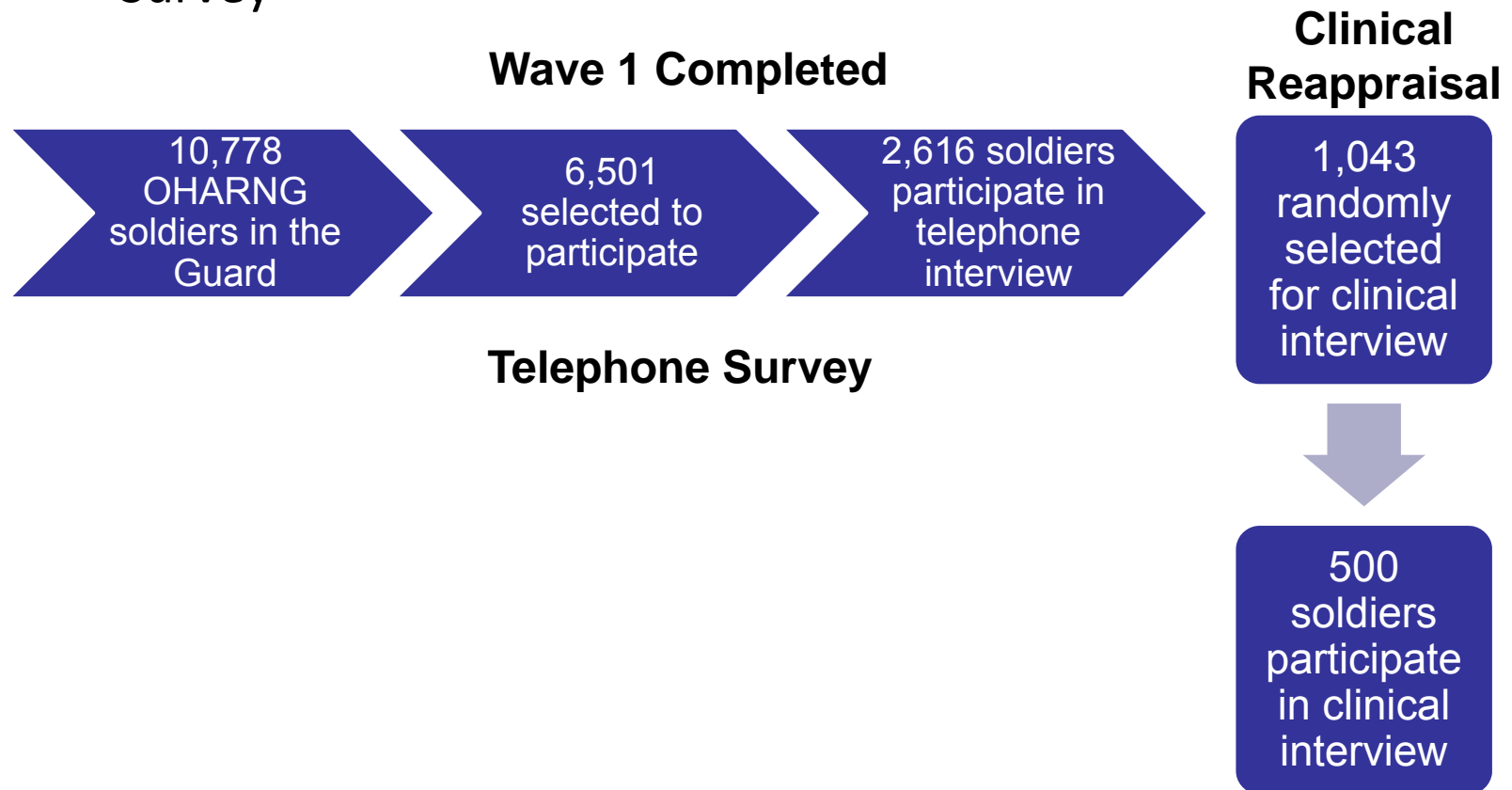
Design and Methodology - Enrollment

| OHARNG MHI | Platform as a Resource for Others |

- ## Scope of Work: Task 1

  - Enrollment not to exceed 3,000 Ohio National Guard Members in the Telephone Survey and 500 for the validation In-Person Survey

Wave 1 Completed

Clinical Reappraisal

| 10,778 OHARNG soldiers in the Guard | 6,501 selected to participate | 2,616 soldiers participate in telephone interview | 1,043 randomly selected for clinical interview |

Telephone Survey

500 soldiers participate in clinical interview

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Design and Methodology – Follow-up

- ## Scope of Work: Task 2
  - Annual participant follow-up, in order to be able to test Specific Aims 1 -3 with associated hypotheses.

Replenishment sample	Wave 2	Wave 3	Wave 4
841 new OHARNG soldiers participate in telephone interview (59.9% cooperation)	1770 OHARNG soldiers completed second telephone interview to date (93.4% cooperation)	1395 OHARNG soldiers completed third telephone interview to date (88.3% cooperation)	1431 OHARNG soldiers completed fourth telephone interview to date (81.8% cooperation)
172 new participants in clinical interview	419 participated in second clinical interview	356 participated in third clinical interview to date	349 participated in fourth clinical interview to date

Design and Methodology - Measures

Core Assessments

New Assessments

Telephone

- **Military History:** Post Deployment Health Assessment (PDHA)
- **General Military Experience:** Deployment Risk and Resilience Inventory (DRRI)
- **TBI:** Military Acute Concussion Evaluation (MACE)
- **General Traumas:** Life Events Checklist (LEC)
- **PTSD:** PTSD Checklist (PCL)
- **Depression:** Patient Health Questionnaire (PHQ-9)
- **GAD:** Generalized Anxiety Disorder-7 (GAD-7)
- **Drug Use:** National Survey on Drug Use and Health (NSDUH)
  - Alcohol
  - Cigarette

Year 2

- **Suicide:** MINI
- **Drug Use:** MINI
  - Marijuana
  - Tranquilizers
- **Hypomania:** MINI
- **Use of Mental Health Services:** Perceived Need for Care Questionnaire (PNCQ)

Year 3

- **Drug Use:** MINI
  - Stimulants
  - Cocaine
  - Narcotics
  - Hallucinogens
  - Inhalants
- **Legal Status:** ASI

Year 4

- **Drug Use:** MINI
  - Painkillers

Clinical

- **Military History:** PDHA
- **General Military Experience:** DRRI
- **Childhood Experiences:** Childhood Trauma Questionnaire (CTQ)
- **Conflict Tactics:** Conflict Tactic Scale (CTS)
- **TBI:** MACE
- **General Traumas:** LEC
- **Suicide:** MINI International Neuropsychiatric Interview
- **Legal Status:** Addiction Severity Index (ASI)
- **Axis I:** Structured Clinical Interview for DSM-IV Disorders (SCID)
- **PTSD:** Clinician Administered PTSD Scale (CAPS)

Year 2

- **Family and Military:** 2000 Survey of Reserve Component Personnel
- **Spiritual Well-Being:** Spiritual Well-Being Scale
- **Resilience:** Resilience Scale
- **Perceived Stress:** Perceived Stress Scale
- **Personal Wellbeing:** Personal Wellbeing Inventory
- **Service Use**
  - Reasons for Seeking Treatment
  - Barriers to Seeking Treatment
- **Family History:** ASI
- **Post Deployment Growth:** Posttraumatic Growth Inventory
- **Suicidal Ideation:** Columbia Suicide Severity Rating Scale
- **Global Assessment of Functioning:** SCID

Year 3

- **Military History:** Unit Questions from 2000 Survey of Reserve Component Personnel
- **Hypervigilance:** Hypervigilance Questionnaire
- **Coping:** Brief Coping Scale
- **Stress:** Perceived Stress Scale
- **Emotion:** Emotion Regulation Questionnaire
- **Aggression:** Buss-Perry Aggression Questionnaire

Year 4

- **Stress:** Response to Stressful Experience Scale
- **Sleep:** Sleep Questionnaire
- **Consumption:** Consumptive Habits Questionnaire
- **Drinking:** Desired Effects of Drinking
- **ADHD:** Adult ADHD Self-Report Scale
- **Social Adjustment:** Social Readjustment Rating Scale

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Design and Methodology – Platform Performance

	Retention (%)	Attrition (%)
Telephone Survey (N = 3457)	64.8	23.2
Clinical Reappraisal (N = 672)	83.2	18.7

Baseline Lifetime Disorder	Sensitivity	Specificity
Deployment-related PTSD	0.50	0.93
Non-deployment related PTSD	0.47	0.94
Major Depressive Disorder	0.35	0.97
Generalized Anxiety Disorder	0.04	0.98
Alcohol Abuse	0.40	0.80
Alcohol Dependence	0.60	0.81
Suicide Risk	0.32	0.87

Prescott, M R e m6 (2013). Prevalence of psychopathology and validation of lay-administered mental health assessments in a large national guard cohort. International Journal of Methods in Psychiatric Research. In Press.

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Study Progress

- **Scope of Work: Task 3 – Academic Productivity**

  - Performance of descriptive analyses on the data collected from the primary and clinical reappraisal sample

  - At least one presentation or peer-reviewed publication per year will be derived from the study data.

Year	Abstracts	Presentations	Accepted Manuscripts	Under Preparation
2009	1	1	0	
2010	12	14	0	
2011	6	6	3	
2012	7	11	5	
2013	4	1	1	9
Total	30	33	9	9

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Study Progress - Publications

In Press & Published Manuscripts:

Title	First Author	Year
PTSD comorbidity and suicidal ideation associated with PTSD within the Ohio Army National Guard – **Journal of Clinical Psychiatry**	**Joseph R. Calabrese, MD**	**2011**
Potentially Modifiable Pre-, Peri-, and Post-deployment Characteristics Associated With Deployment-Related Posttraumatic Stress Disorder Among Ohio Army National Guard Soldiers - **Annals of Epidemiology**	**Emily Goldmann, PhD**	**2011**
Coincident posttraumatic stress disorder and depression predict alcohol abuse during and after deployment among Army National Guard soldiers – **Drug and Alcohol**	**Brandon D. Marshall, PhD**	**2011**
The factor structure of major depression symptoms: A test of four competing models using the Patient Health Questionnaire-9 – **Psychiatry Research**	**Jon D. Elhai, PhD**	**2012**
Posttraumatic stress disorder and HIV risk behavior among Army National Guard soldiers: The mediating role of depression. – **Journal of Traumatic Stress**	**Brandon D. Marshall, PhD**	**2012**
Cigarette smoking and subsequent risk of suicidal ideation among National Guard Soldiers – **Journal of Affective Disorders**	**Renee D. Goodwin, PhD**	**2012**
Does smoking predict depression onset among military personnel? – **Psychiatry Research**	**Renee D. Goodwin, PhD**	**2012**
Relations between the underlying dimensions of PTSD and major depression using an epidemiological survey of deployed Ohio National Guard soldiers – **Journal of Affective Disorders**	**Tracy L. Biehn**	**2012**
Validation of lay-administered mental health assessments in a large Army National Guard cohort – **International Journal of Methods in Psychiatric Research**	**Marta R. Prescott, PhD**	**2013**

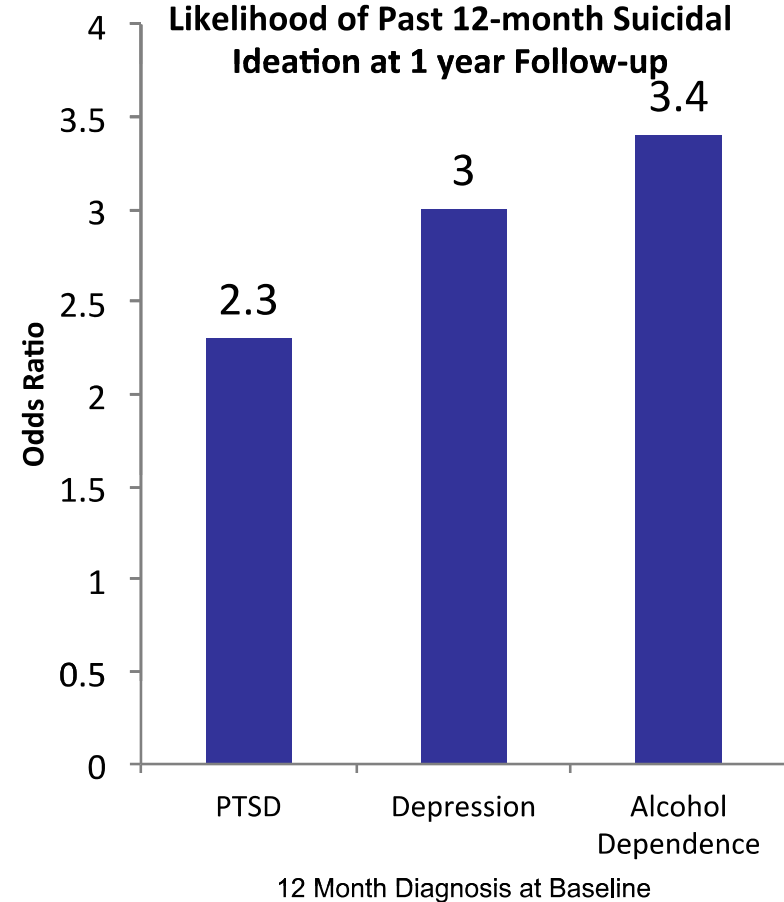# Study Findings – Alcohol (Blow et al Under Review)

OHARNG MHI → Platform as a Resource for Others

Probability of peri- and post-deployment alcohol abuse

Conditional Probability of Alcohol Abuse First Occuring During/Following Deployment

No PTSD or Depression	PTSD Only	Depression Only	Both PTSD and Depression
7.0%	16.7%	22.6%	43.8%

Presence of Condition(s) first occuring During/Following Deployment

Likelihood of Past 12-month Suicidal Ideation at 1 year Follow-up

Odds Ratio

PTSD	Depression	Alcohol Dependence
2.3	3	3.4

12 Month Diagnosis at Baseline

Marshall, B. D., et al. (2012). Coincident posttraumatic stress disorder and depression predict alcohol abuse during and after deployment among Army National Guard soldiers. Drug and alcohol dependence. **Note:** PTSD and Depression defined as first occurring during or following deployment

Cohen, G.H., Prescott, M. R., Liberzon, I., Tamburrino, M. B., Calabrese, J. R., & Galea, S. (Under Preparation). Alcohol Dependence and Incident Suicidal Ideation
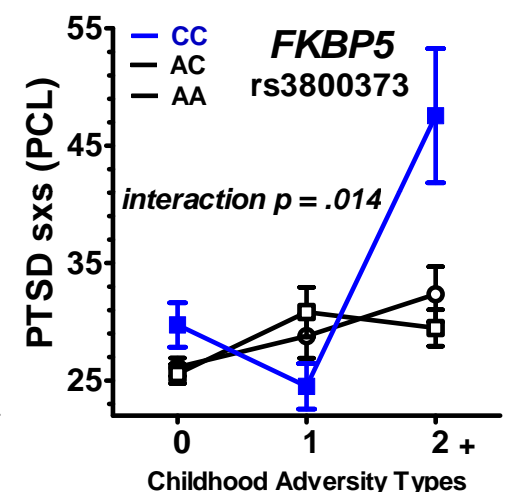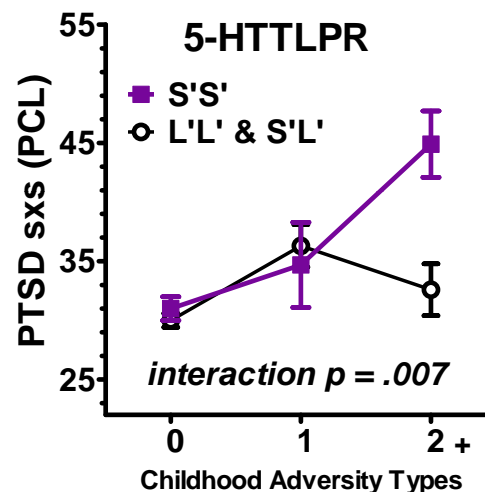
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Study Findings - Genotyping

- **82% consented, 1042 soldiers** returned specimens (Oragene kits) to lab
- **Genotyping:** 5-HTTLPR w/PCR, >3200 SNPs in candidate genes w/ Illumina array.
- Initial analyses N=854, N=57 no LT trauma; **N=715 European ancestry by PCA**

Replications:

G x E (childhood trauma)

- *No "main effects" association w/PTSD*
- **Gene x Childhood trauma interaction in 5-HTTLPR and *FKBP5***
- Serotonin Transporter promoter "triallelic" **5-HTTLPR p = .007**
- *FKBP5* (rs3800373) **p = .017**

Novel findings:

- *No "main effects" SNP association w/ PTSD sxs*
- **Gene x Childhood adversity interaction *ADRB2***
  (beta2 Adrenergic receptor gene)
  - **rs2400707 p = 1.0 x 10-5**
  - **rs11168068 p = 1.4 x 10-5**
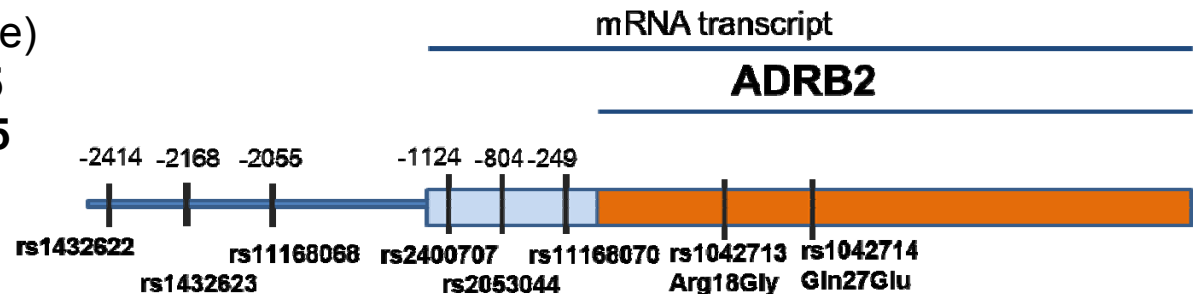
Expenditures & Future Plans

FY06-FY11 Congressional Allocations:

Current Budget	Expended Funds	%
$12,308,000	$10,959,119	89%

As of 12/31/2012

Plans for 2013-2018:
- Project is funded through 9/27/ 2013
- BAA full proposals submitted 2/6/2013 for the platform and alcohol
- Genetics and mTBI biomarkers submission pending funding

Activities CY	12	13	14	15	16	17	18
Analysis/Manuscript Preparation		8 Manuscripts					
Platform Data Collection			Data Collection, Analyses, Manuscript Preparation				
Alcohol Intervention/Prevention			Data Collection, Analyses, Manuscript Preparation				
Genetics Repository							
mTBI Biomarkers			Collaboration targeting biomarker collection for mTBI, PTSD, or both				

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OHARNG MHI Future Directions

• Position project as a platform for the conduct of projects co-led by other expert investigators around the country.

• Initiate a parallel project using the platform to study pre-, peri-, and post-deployment factors associated with the lifetime trajectory of mTBI.

• Target the development of a collaboration that will focus on biomarker collection to contrast subjects with mTBI, PTSD, or both.

• Unique assets of the project:
  – Population based with minimal selection bias
  – Availability of an in-person sample with high rates of study retention (80-90%).

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public service extends into his community, where he serves as a deacon in his church, uses his vacation to chaperone youth trips, and donates his time to coaching soccer. His devotion to faith and family is recognizable to all who have had the privilege to know Jerry and work beside him. He attributes much of his success to his wife, Karen, his children, and his eight grandchildren, who have always been fully supportive of his career. Jerry once claimed: "I don't come to work to work. I love what I do."

On behalf of the U.S. House of Representatives, I congratulate Jerry on his retirement and thank him for his dedication and outstanding contributions to the institution. I wish him the best in all his future endeavors.

HONORING CATHY KIMBROUGH

HON. BENNIE G. THOMPSON
OF MISSISSIPPI
IN THE HOUSE OF REPRESENTATIVES
Thursday, June 13, 2013

Mr. THOMPSON of Mississippi. Mr. Speaker, I rise today to honor a remarkable public servant, Mrs. Cathy Kimbrough.

Mrs. Kimbrough has served adults and children in numerous capacities. Some of the service areas include: reading instructor, while in Germany; General College reading instructor at Alcorn State University; and self-contained and inclusion teacher in the Attala County School District.

Mrs. Kimbrough has served her community as local president of the Attala County Association of Educators and has also served on the Board of Directors for the Boys' and Girls' Club in Kosciusko/Attala County.

Mrs. Kimbrough is a member of the following organizations: Order of the Eastern Star, National Council of Negro Women, and Alpha Kappa Alpha Sorority, Incorporated. She is also a member of Pleasant Hill M.B. Church, pastured by Rev. Osie C. Grays.

Mrs. Kimbrough earned her bachelor's and master's degrees from Jackson State University. She was a member of the Phi Kappa Phi Honor Society and the Alpha Beta Alpha Library Science Fraternity.

Mrs. Kimbrough is married to Mr. Henry Kimbrough and has four children: Jerry Jr. (Erica), Essence Crystal (Theodore), Sonja Merrie', and Joyanne' Faith; six grandchildren—Deontrez Jerrick, Jersia, Kamiah, Kayla and Shytianna. She enjoys creating song lyrics, writing poetry, reading and fishing.

Mr. Speaker, I ask my colleagues to join me in recognizing Mrs. Cathy Kimbrough for her dedication to serving others in Attala County.

PERSONAL EXPLANATION

HON. LOUISE McINTOSH SLAUGHTER
OF NEW YORK
IN THE HOUSE OF REPRESENTATIVES
Thursday, June 13, 2013

Ms. SLAUGHTER. Mr. Speaker, I was unavoidably detained and missed rollcall vote numbers 214, 215, and 216. Had I been present, I would have voted "no" on rollcall vote number 214 and "yes" on rollcall vote numbers 215 and 216.

RECOGNIZING THE REMARKABLE ACHIEVEMENTS OF JOSEPH CALABRESE, MD

HON. MARCY KAPTUR
OF OHIO
IN THE HOUSE OF REPRESENTATIVES
Thursday, June 13, 2013

Ms. KAPTUR. Mr. Speaker, I rise today to acknowledge the outstanding accomplishments of Doctor Joseph Calabrese, professor of psychiatry at Case Western Reserve University and director of the Mood Disorders Program at University Hospitals Case Medical Center in Cleveland. Doctor Calabrese recently gained international acclaim when he was presented with the Lifetime Achievement Award by the European Bipolar Forum at its annual meeting in Seville, Spain.

The accolades are well deserved—and I speak from personal experience—because Doctor Calabrese has taken the lead role in a major initiative that I helped launch under the auspices of the U.S. Department of Defense to study the effects of post-traumatic stress disorder on soldiers returning from combat zones. I have watched as Doctor Calabrese, working in concert with doctors at the University of Toledo, has conducted truly groundbreaking research involving combat veterans who suffer from PTSD.

As a member of the Defense Subcommittee of House Appropriations, I have long been concerned about the incidence of suicide among our combat veterans. In communities and families throughout our country, we have seen the devastating impact of PTSD. The ambitious research project by Doctor Calabrese that I have been privileged to support has studied the relationship between PTSD and suicidal ideation among members of the Ohio Army National Guard.

After completing a research fellowship at the National Institute of Mental Health, Doctor Calabrese returned to Cleveland to start the Mood Disorders Program. He also co-directs, along with Doctor Robert Finding, M.D., the NIMH-funded Bipolar Research Center in Cleveland. Doctor Calabrese has been the recipient of no fewer than five federal research grants from the NIMH. The Mood Disorders program at University Hospitals Case Medical Center was designated as a Center of Excellence under Dr. Calabrese's exceptional leadership.

Dr. Calabrese has dedicated his work to the improvement of clinical outcomes in underserved populations of bipolar disorder, including people who receive care at community health centers, children, adults, older adults, those in prison and those currently abusing alcohol or drugs. His research reflects a caring nature and true gift of service.

During the course of his career, Doctor Calabrese has published more than 300 peer-reviewed papers. He is a member of a number of scientific advisory boards and is affiliated with the American Psychiatric Association.

I am proud to support his clinical efforts and his exemplary service to the Cleveland community, our nation, and veterans everywhere. I am pleased to commend Doctor Joseph Calabrese on the occasion of his receipt of the European Bipolar Forum's Lifetime Achievement Award and thank him for his noble work.

RECOGNIZING THE SYRACUSE VA MEDICAL CENTER'S DIAMOND JUBILEE 1953–2013

HON. DANIEL B. MAFFEI
OF NEW YORK
IN THE HOUSE OF REPRESENTATIVES
Thursday, June 13, 2013

Mr. MAFFEI. Mr. Speaker, it is with great pride that I rise today to recognize the Syracuse VA Medical Center's Diamond Jubliee.

The Syracuse VA Medical Center, Located at 800 Irving Avenue, first opened its doors on June 14th, 1953. For the past 60 years, the medical center has dedicated itself to providing superior care to veterans and their families. Part of VA Healthcare Upstate New York, the Syracuse VA Medical Center provides outpatient support to the greater Central New York area by operating community clinics in Auburn, Binghamton, Cortland, Massena, Oswego, Rome, and Watertown. The staff should be commended for their dedication and commitment to those who have served this nation.

The Syracuse VA Medical Center has been recognized by the Department of Veterans Affairs as a Center of Excellence for its Operation Enduring Freedom, Operation Iraqi Freedom, and Polytrauma Programs. Additionally, the center is also the primary referral center for neurosurgery and urological renal stone treatment, which encompasses all of upstate New York and Northern Pennsylvania veterans.

On June 14, 2013, the Syracuse VA Medical Center will formally open their Spine Cord Injury & Disorder Center. This state-of-the-art center provides expanded services that our veterans deserve. The facility will serve veterans across Upstate New York who now travel to New York City or out of state to get spinal cord care. Our veterans deserve the best care this nation has to offer, and with the six-floor addition, the Syracuse VA Medical Center will continue to do just that.

To mark this special occasion, Secretary of Veterans Affairs Eric K. Shinseki will be present to deliver the keynote speech for the occasion. It is truly an honor to have Secretary Shinselci present to celebrate this momentous occasion.

Mr. Speaker, I ask my colleagues to join with me in recognizing the Syracuse VA Medical Center's Diamond Jubilee event, and wish the center many more years of continued growth and success in its service of the veteran community of Central New York.

HONORING DAN SPENCER FOR HIS INDUCTION INTO THE "MUMMERS HALL OF FAME"

HON. ROBERT E. ANDREWS
OF NEW JERSEY
IN THE HOUSE OF REPRESENTATIVES
Thursday, June 13, 2013

Mr. ANDREWS. Mr. Speaker, I rise today to honor Dan Spencer for his immense contributions to the string band community in South Jersey. For the past forty-one years, Mr. Spencer has diligently served as an active leader and has promoted success in numerous string band and mummers associations across New Jersey.

Military Mental Health:
Focus on the Ohio Army National Guard Mental Health Initiative

Joseph R. Calabrese, MD
Coordinating Principal Investigator
Joseph.calabrese@uhhospitals.org

University Hospitals
Case Medical Center

SCHOOL OF MEDICINE
CASE WESTERN RESERVE
UNIVERSITY

1

Co-PIs & Acknowledgements

Columbia University
Scientific Principal Investigator – Sandro Galea, MD, DrPH

Ann Arbor VA
Dir., Translational Research - Israel Liberzon, MD

University of Toledo (UT)
Co-PI – Marijo Tamburrino, MD

Michigan State University
Co-Investigator Director of Informatics - Philip Reed, PhD, MS

Abt. SRBI, Inc
Telephone Survey Data Collection Firm – Mark Morgan

Ohio National Guard

TAG Deborah Ashenhurst	**Jeremy Kauffman, PsyD**	**Colonel Julie Blike**
ATAG John Harris	**Captain Sephan Frazier**	

2

Recent Increased Involvement of the National Guard

National Guard is increasingly used in combat zones and overseas operations

- 18% of the Persian Gulf War

- ~40% of the total operating force in Operation Iraqi Freedom (OIF) and Operation Enduring Freedom (OEF)

- From 9/11/01 until March 2009, 401,840 National Guard Soldiers have been mobilized or called up for duty

3

Differences Between Reserve and Active Components

Uniqueness of the National Guard

- Balance civilian job with deployment

- Deployed separately from their unit they trained with

- Manage disaster relief missions

- Only time-limited health insurance

- Less access to support services, but play a major role in combat, now contributing >1/3 of combat forces.

4

Limited Data on Long-term Mental Health

Mental Health of National Guard Soldiers

- Little known regarding the course of mental health over time

- Pre-, peri-, post- analytic framework not typically used to understand events across the life course.

- Study of trajectories useful to understand individual course and outcome over time.

- Very little work on trajectories due to the requirement long-term follow-up.

5

OHIO ARMY NATIONAL GUARD MENTAL HEALTH INITIATIVE

6

OHARNG MHI Background & Rationale

Existing Efforts

- 1st <u>prospective study to use pre- and peri- deployment Guard data</u> to meet the real-time prioritized translational needs of vulnerable subgroups.

Uniqueness

- Focus on how pre-, peri-, and post-deployment factors jointly <u>predict distinct trajectories</u> of posttraumatic psychopathology
- Focus on how interpersonal, intrapersonal, and contextual factors jointly <u>predict distinct trajectories</u> of posttraumatic psychopathology
- Focus on how both <u>military</u> and <u>civilian</u> experiences shape longitudinal risk for psychopathology.
- 1st <u>study</u> to generate an association with PTSD symptoms in soldiers deployed to <u>Iraq and Afghanistan</u>, while replicating previous findings of G x E interaction effects in FKBP5 and 5-HTTLPR (ACNP 2012)
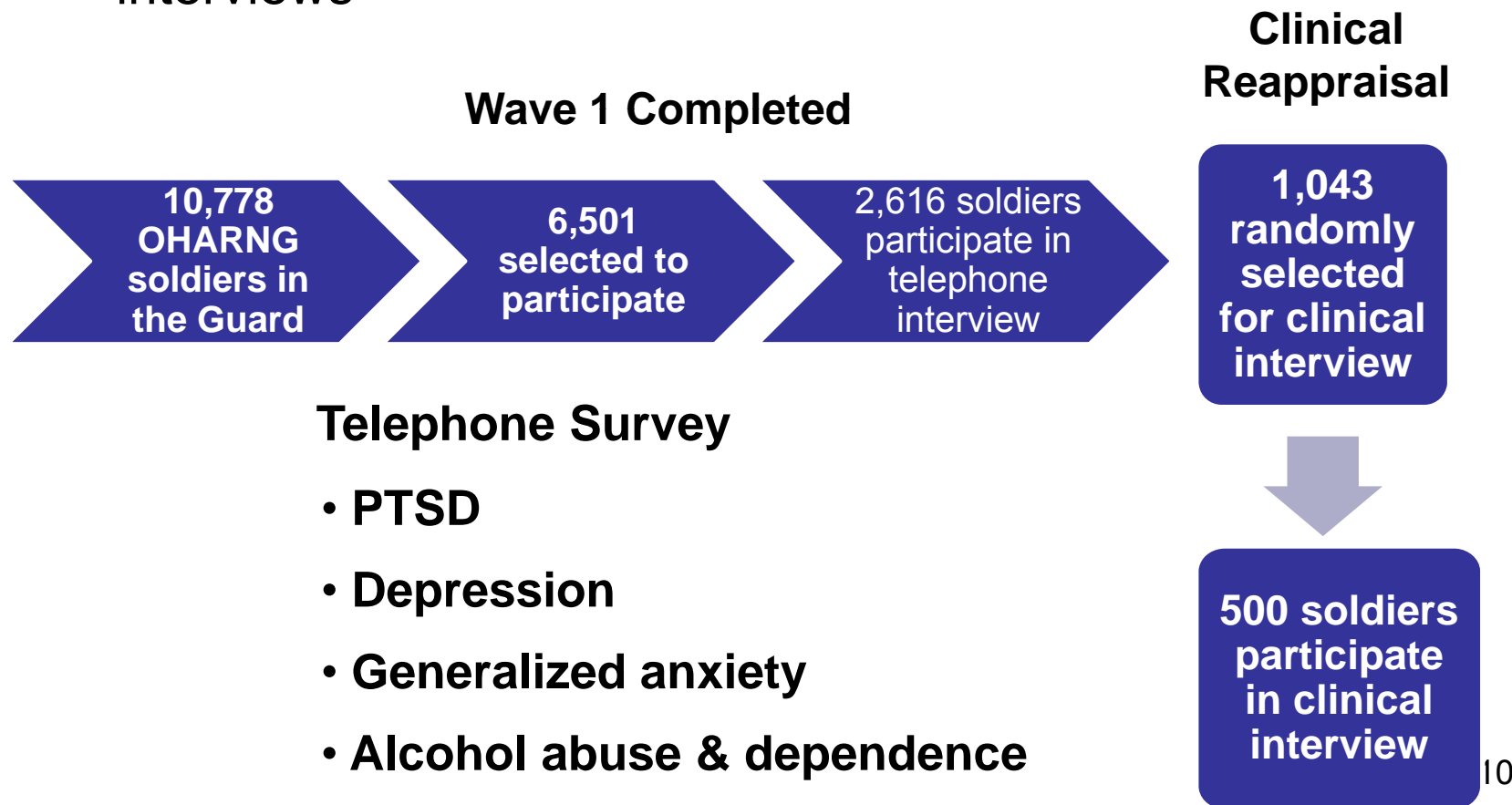
Value

- <u>Feedback from leadership</u> has led to a 2013 submission targeting the development of a <u>secondary prevention</u> study targeting hazardous <u>alcohol use in soldiers not yet deployed</u> (Fred Blow-currently under review)
- <u>Study results led to revisions</u> of the Ohio Guard's Suicide Prevention Training Program using new data highlighting the relationship between suicide and Axis I comorbidity (Calabrese et al 2011)

7

OHARNG MHI Study Value

- Genetics Repository
  N = 1088
  Liberzon

- Neuroimaging Pilot Study
  N = 41
  Liberzon/Wang

- Telephone Project
  N = 3457

- Alcohol Prevention Study
  N = 850
  Blow
  (Under Review)

- Field Deployed Tele-Diagnosis
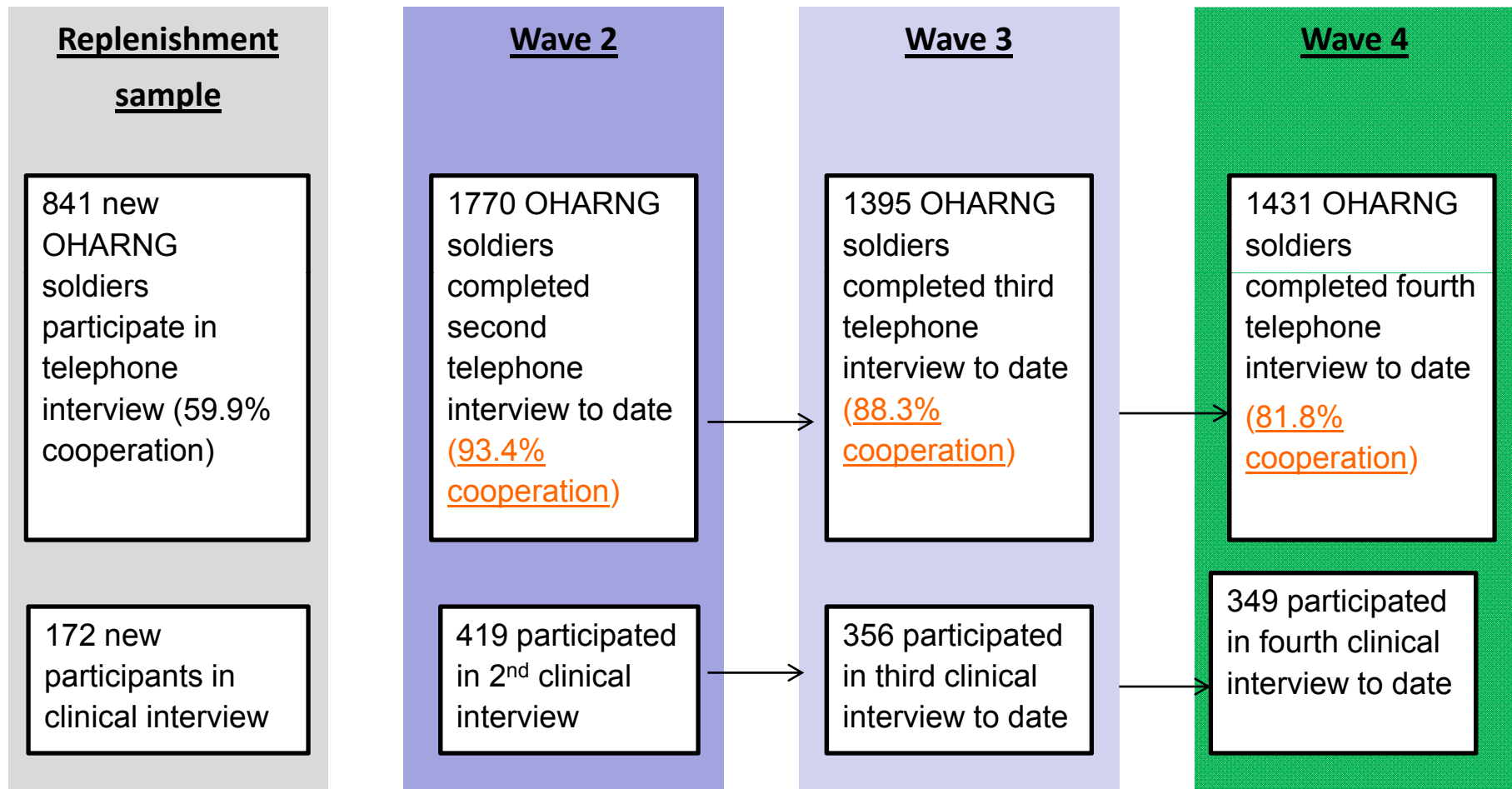 Intelligent Automation, Inc.
  Xu

8
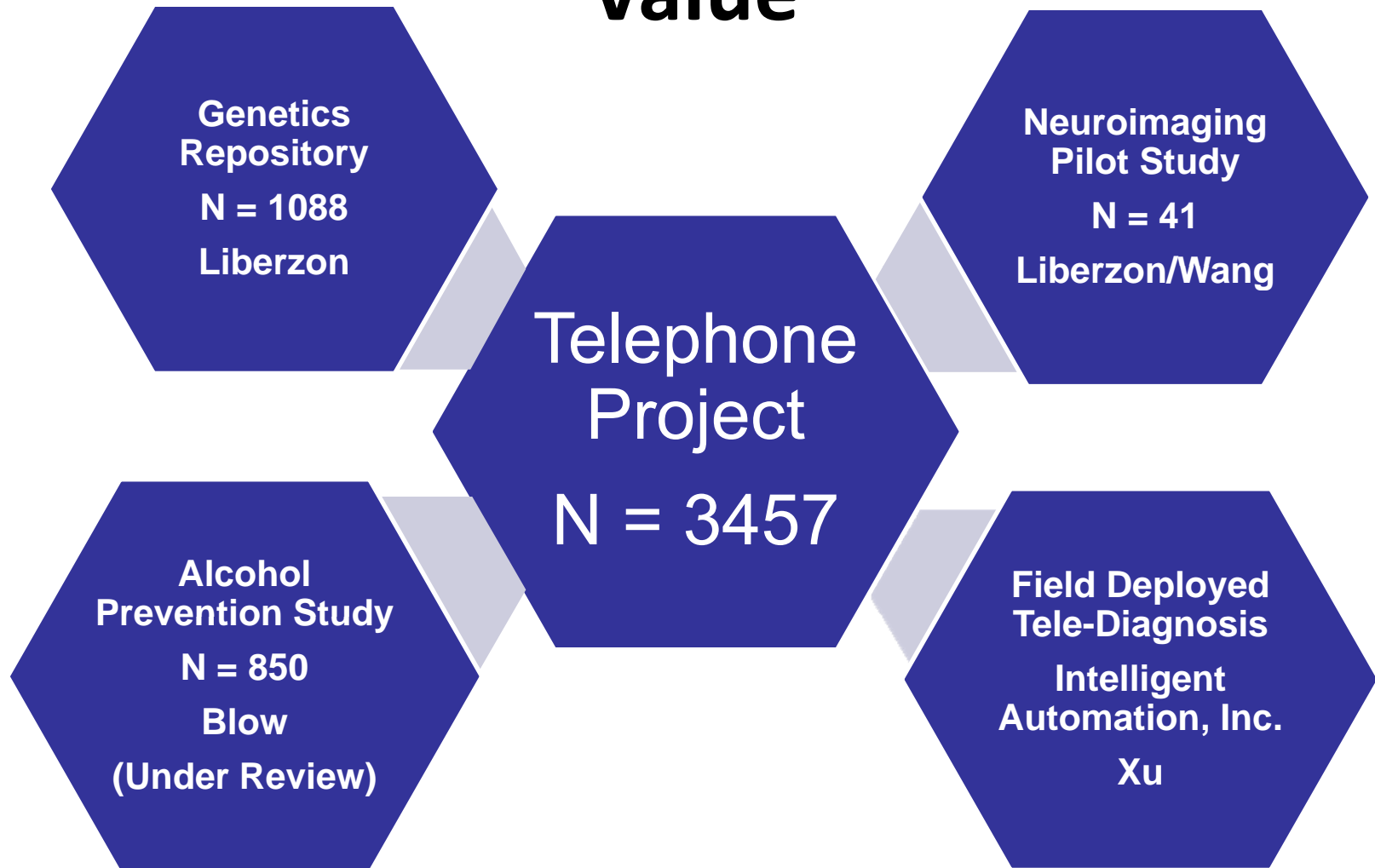
Design and Methodology – Study Enrollment

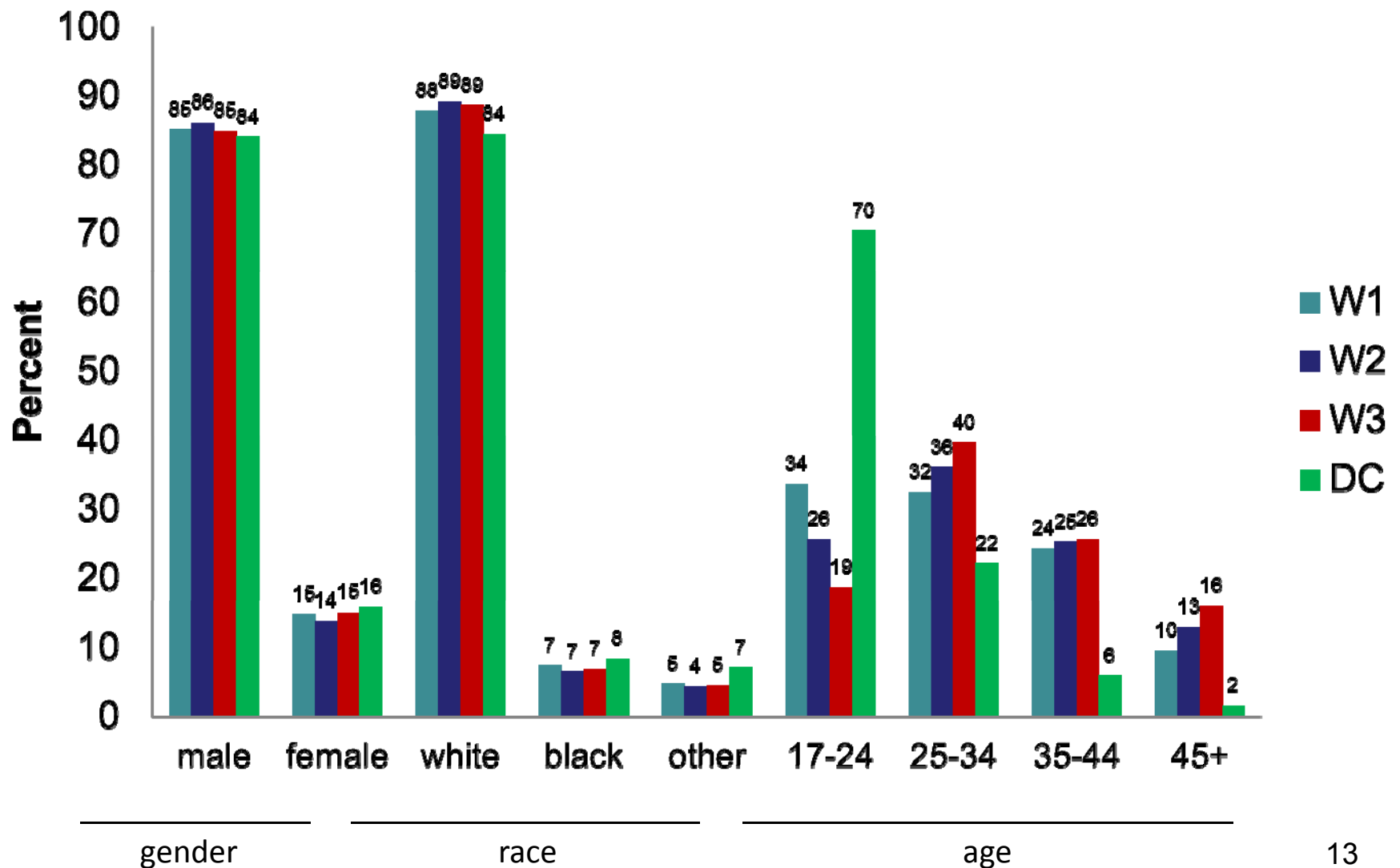– Enrollment of 3,000 Ohio Army National Guard in the Telephone Survey and 500 of who received In-Person interviews

Wave 1 Completed

Clinical Reappraisal

| 10,778 OHARNG soldiers in the Guard | 6,501 selected to participate | 2,616 soldiers participate in telephone interview | 1,043 randomly selected for clinical interview |

500 soldiers participate in clinical interview

Telephone Survey

- **PTSD**

- **Depression**

- **Generalized anxiety**

- **Alcohol abuse & dependence**

10

Design and Methodology: Follow-Up

Replenishment sample	Wave 2	Wave 3	Wave 4
841 new OHARNG soldiers participate in telephone interview (59.9% cooperation)	1770 OHARNG soldiers completed second telephone interview to date (93.4% cooperation)	1395 OHARNG soldiers completed third telephone interview to date (88.3% cooperation)	1431 OHARNG soldiers completed fourth telephone interview to date (81.8% cooperation)
172 new participants in clinical interview	419 participated in 2nd clinical interview	356 participated in third clinical interview to date	349 participated in fourth clinical interview to date

11

Characteristics of the Study Sample

Majority of participants are young, white, males

Telephone Survey Sample. W = Wave

Majority of participants are married and enlisted

Telephone Survey Sample

14
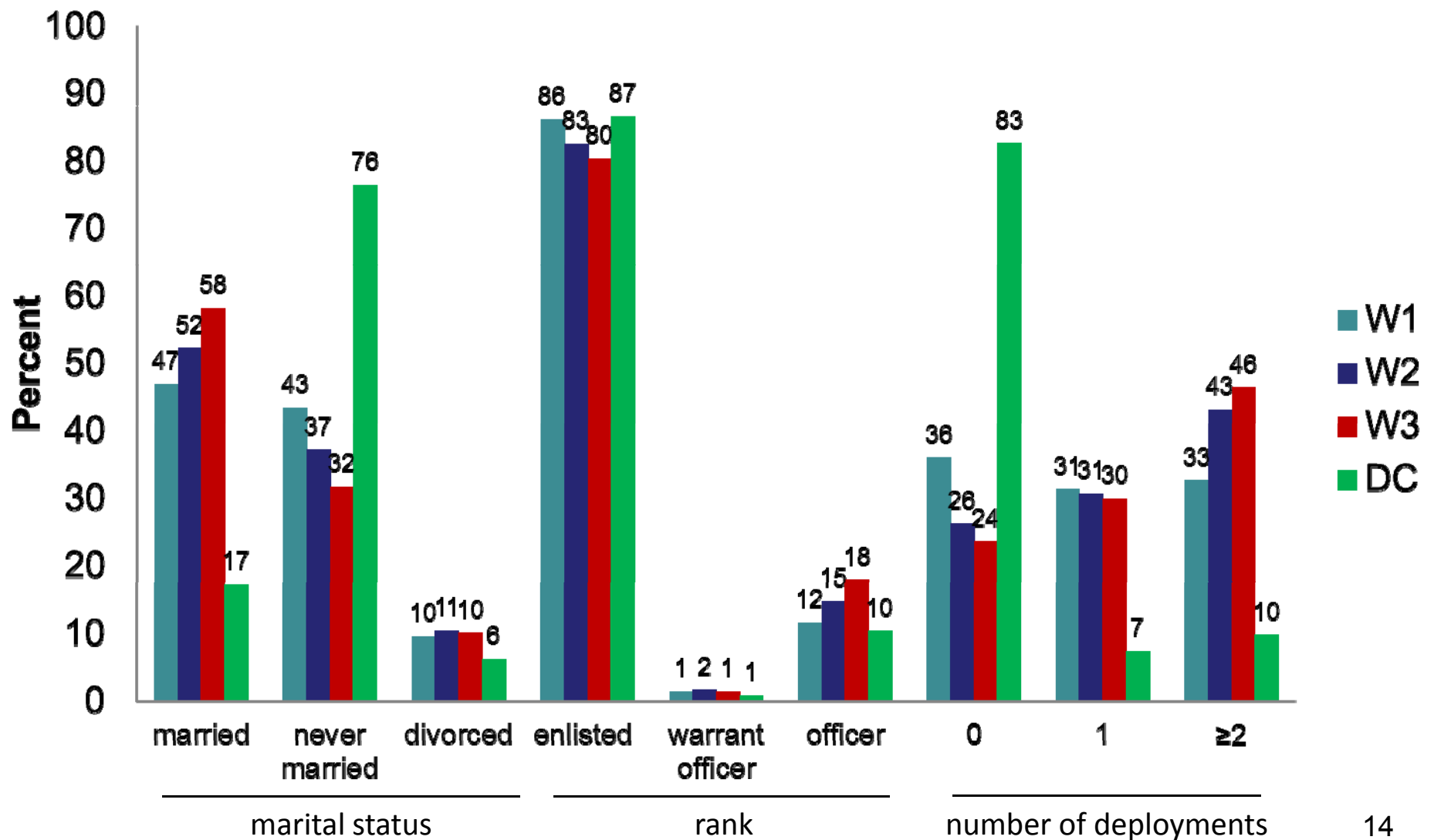
Telephone Survey – Prevalence Rates

15%, 26%, & 58% of soldiers had history of at least one of the 5 conditions
(past 30d, past year, and lifetime respectively)

Past 30 days

12% 3%

85%

Past year

7%

19%

74%

Lifetime

17%

42%

41%
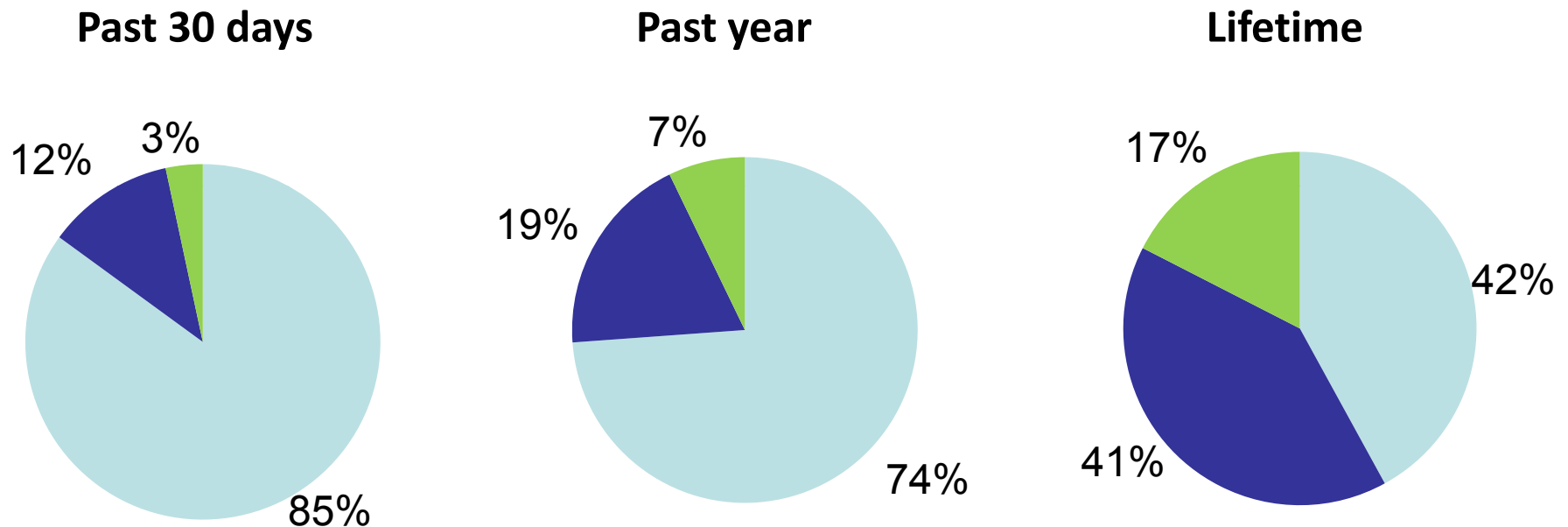
"Single time-point prevalence rates can be very difficult to interpret."

No disorder   One disorder   At least two disorders

Alcohol abuse or dependence are similarly prevalent lifetime disorders

Telephone Survey Sample: N = 1,164. Alcohol Use Disorder = alcohol abuse and alcohol dependence.
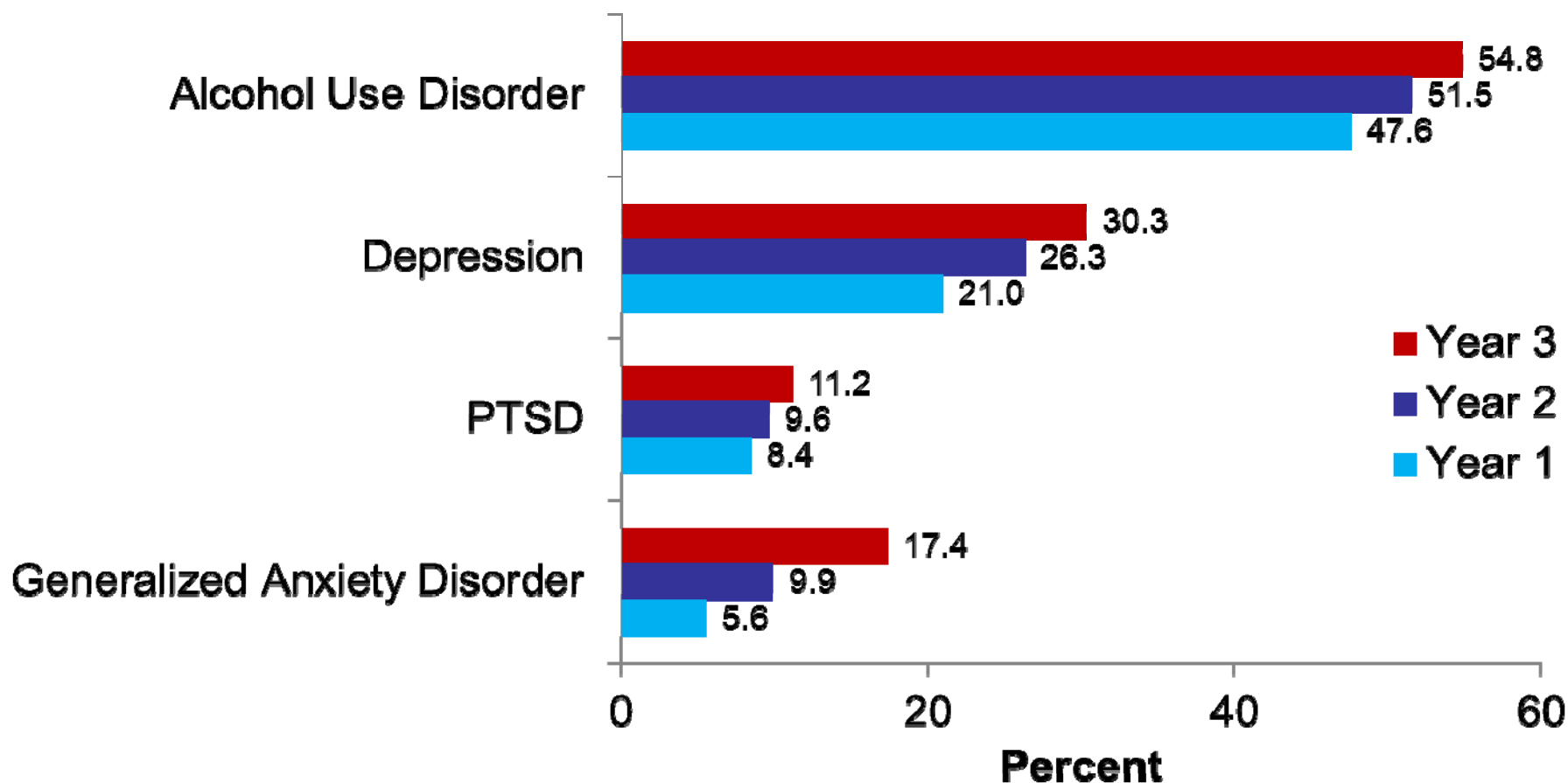
Depression and alcohol abuse/dependence most prevalent in past year

Telephone Survey Sample: N = 1164

18
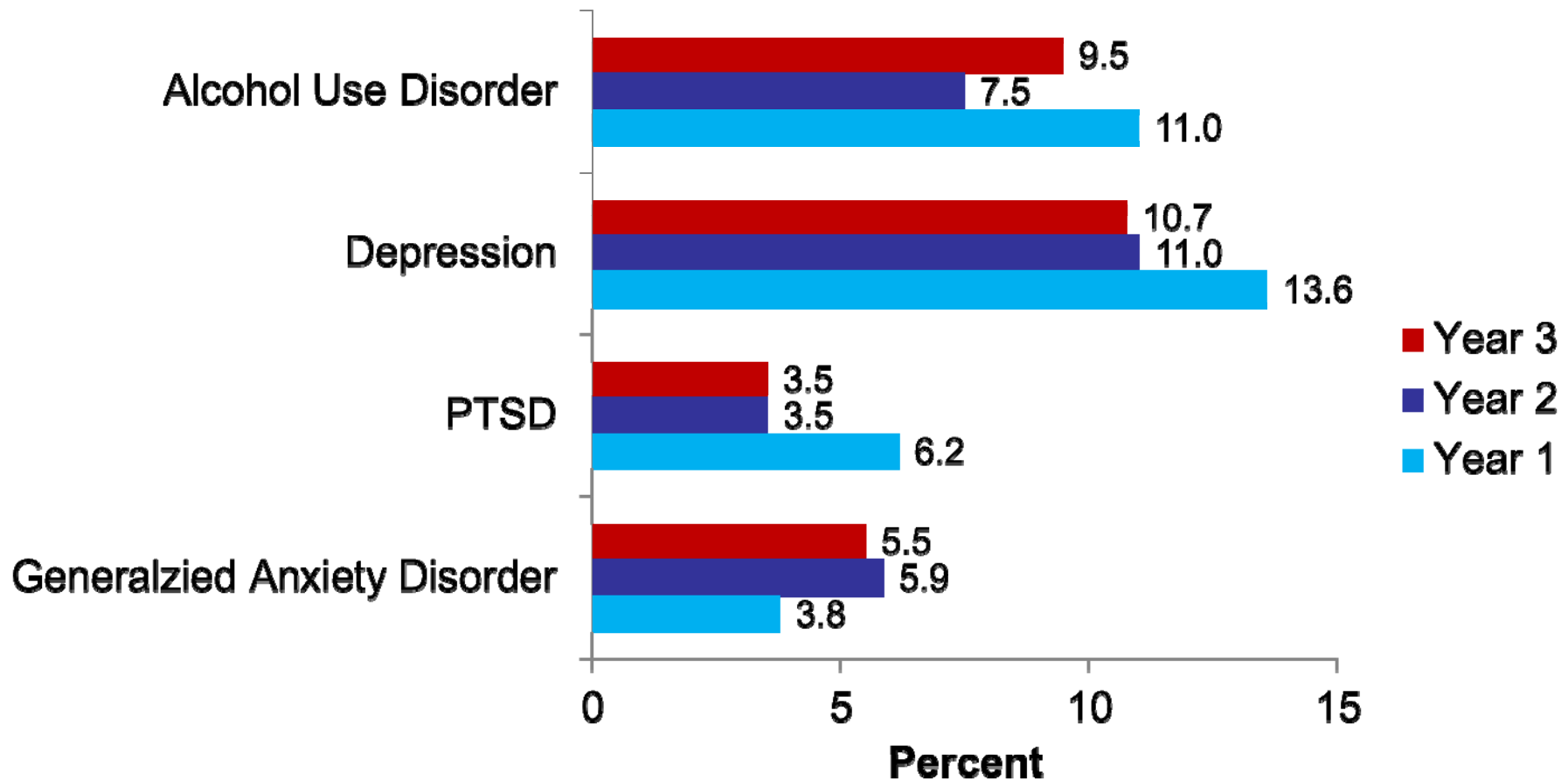
Depression and alcohol abuse/dependence is most prevalent over two years

* N = 491 participants who did not have a mental health disorder at baseline and were present for all three waves of the study
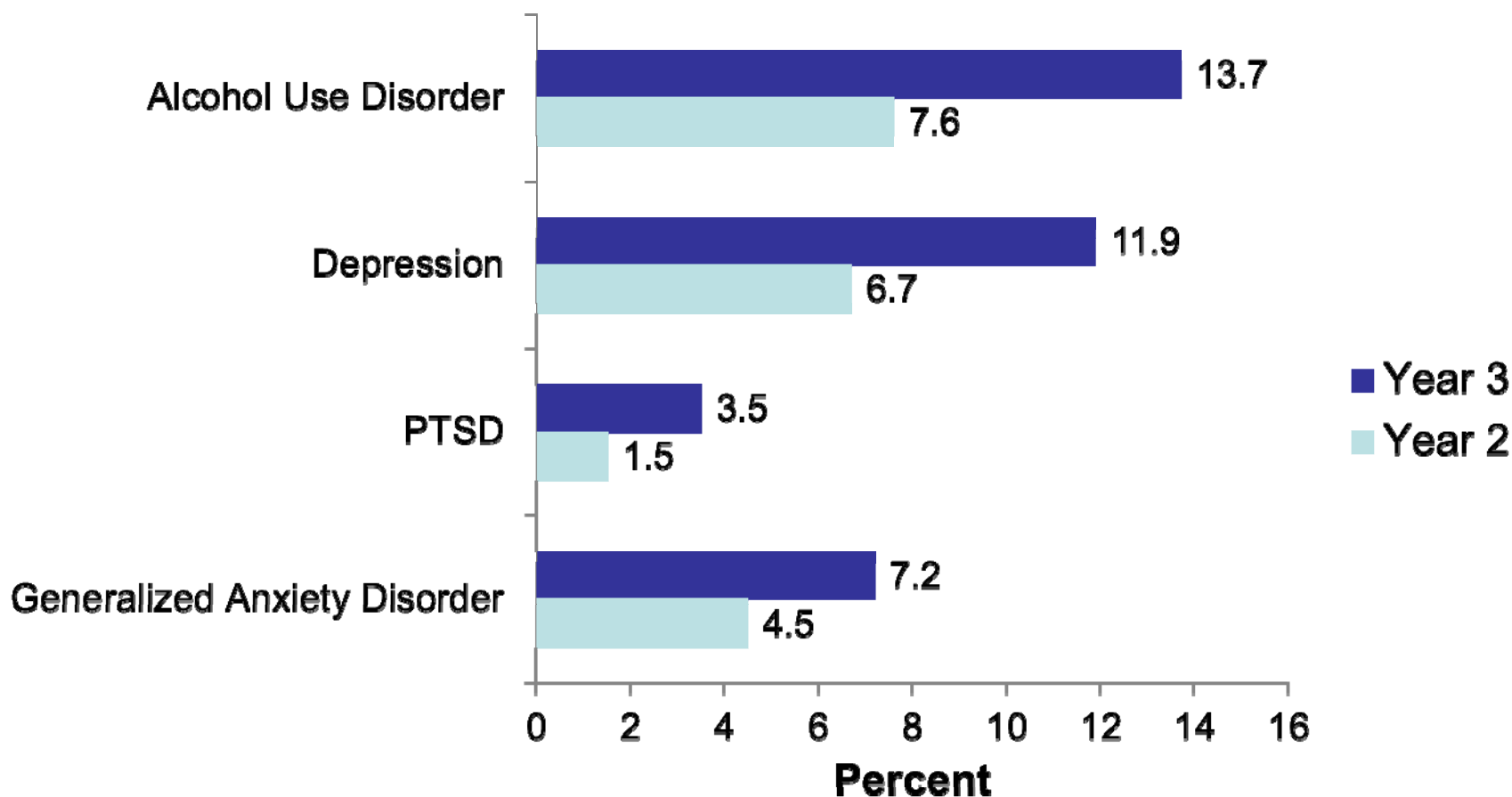
CONCLUSIONS

- Overall, rates of PTSD do not appear to be markedly increased within the OHARNG compared to rates that would otherwise be expected in a similar age group.

- However, there appear to be <u>vulnerable subgroups</u> and within these subgroups, rates of these 5 conditions are increased.

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Vulnerable Subgroups

1. PTSD comorbidity and suicidal ideation
2. Post-deployment support and PTSD
3. Alcohol dependence and depression
4. PTSD and depression
5. HIV risk behavior, PTSD, depression, and History of alcohol use disorders
6. Cigarette smoking and suicidal ideation
7. Cigarette smoking and depression
8. Prior sexual trauma, PTSD, and depression

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PTSD Comorbidity and Suicide Ideation

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Soldiers with PTSD are 5 Times More Likely to Have Lifetime Suicidality
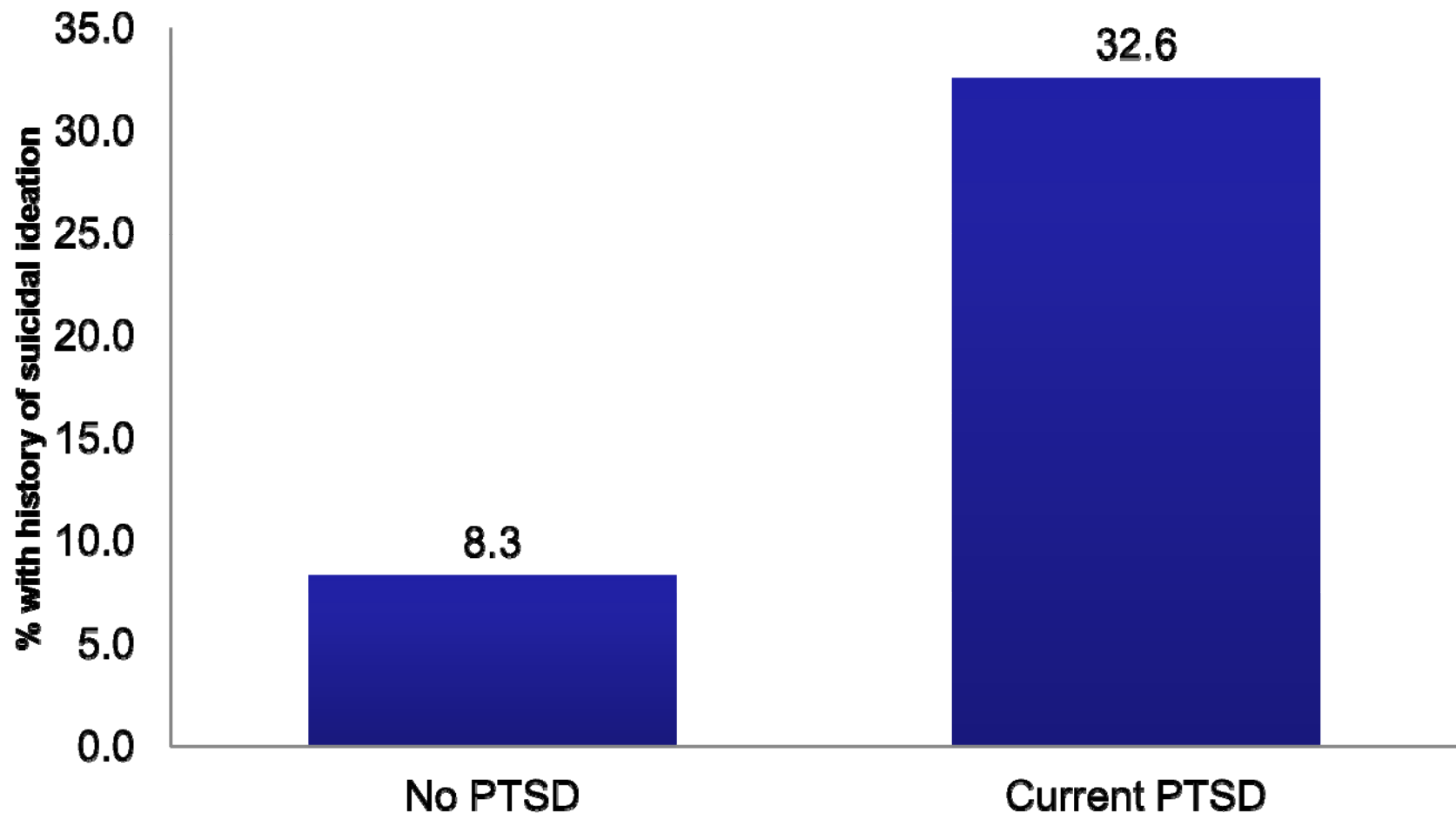
Calabrese JR Prescott M, Tamburrino M, Liberzon I, Slembarski R, Goldman E, Shirley E, Fine T, Goto T, Wilson K, Ganocy S, Chan P, Serrano MB, Sizemore J, Galea S: PTSD Comorbidity and Suicidal Ideation Associated with PTSD Within the Ohio Army National Guard. *J Clin. Psychiatry* 2011; 72(8): 1072-1078.

Comorbid PTSD and Lifetime Suicidality
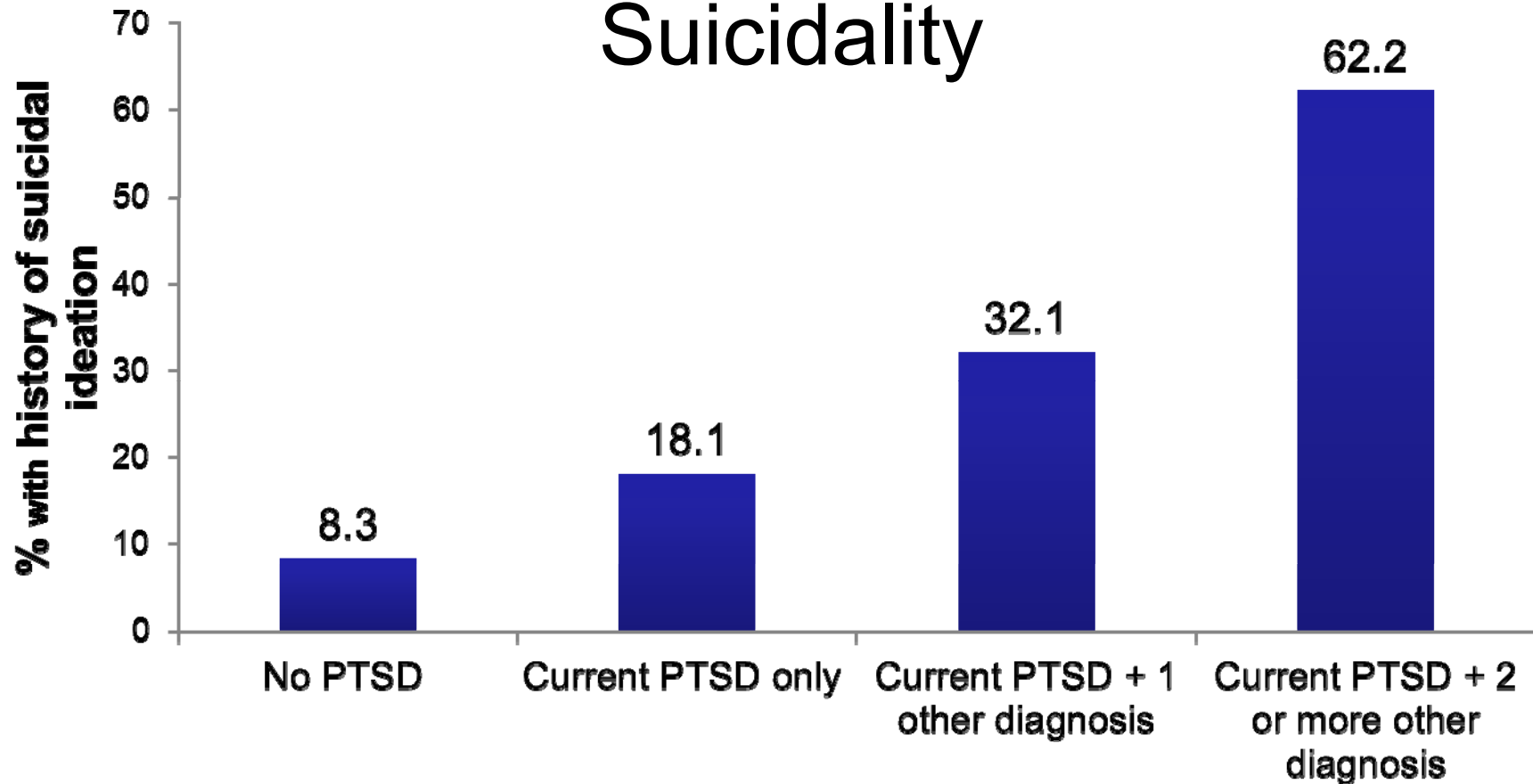
- **Soldiers with PTSD and $\geq$ 2 are almost 8 times more likely to report suicidality than those without PTSD.**

Calabrese JR Prescott M, Tamburrino M, Liberzon I, Slembarski R, Goldman E, Shirley E, Fine T, Goto T, Wilson K, Ganocy S, Chan P, Serrano MB, Sizemore J, Galea S: PTSD Comorbidity and Suicidal Ideation Associated with PTSD Within the Ohio Army National Guard. *J Clin. Psychiatry* 2011; 72(8): 1072-1078.

Post Deployment Support and PTSD

28

Only combinations that included "high post-deployment social support" led to resilience
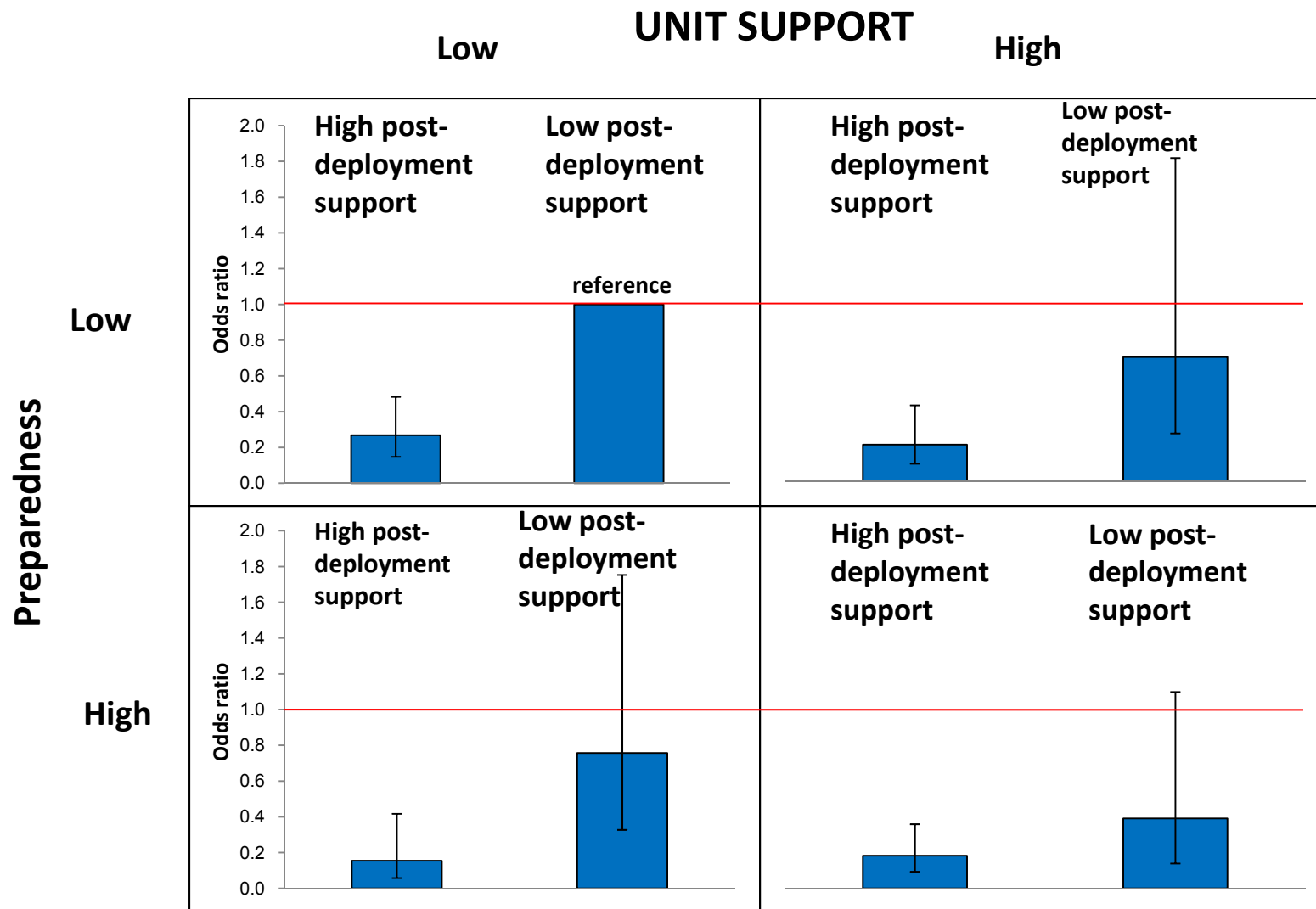
Goldmann E, Calabrese J, Prescott M, Tamburrino M, Liberzon I, Slembarski R ... & Galea, S. (2012). Potentially modifiable pre-, peri-, and post-deployment characteristics associated with deployment-related posttraumatic stress disorder among Ohio army national guard soldiers. *Annals of Epidemiology*, 22(2), 71-78.
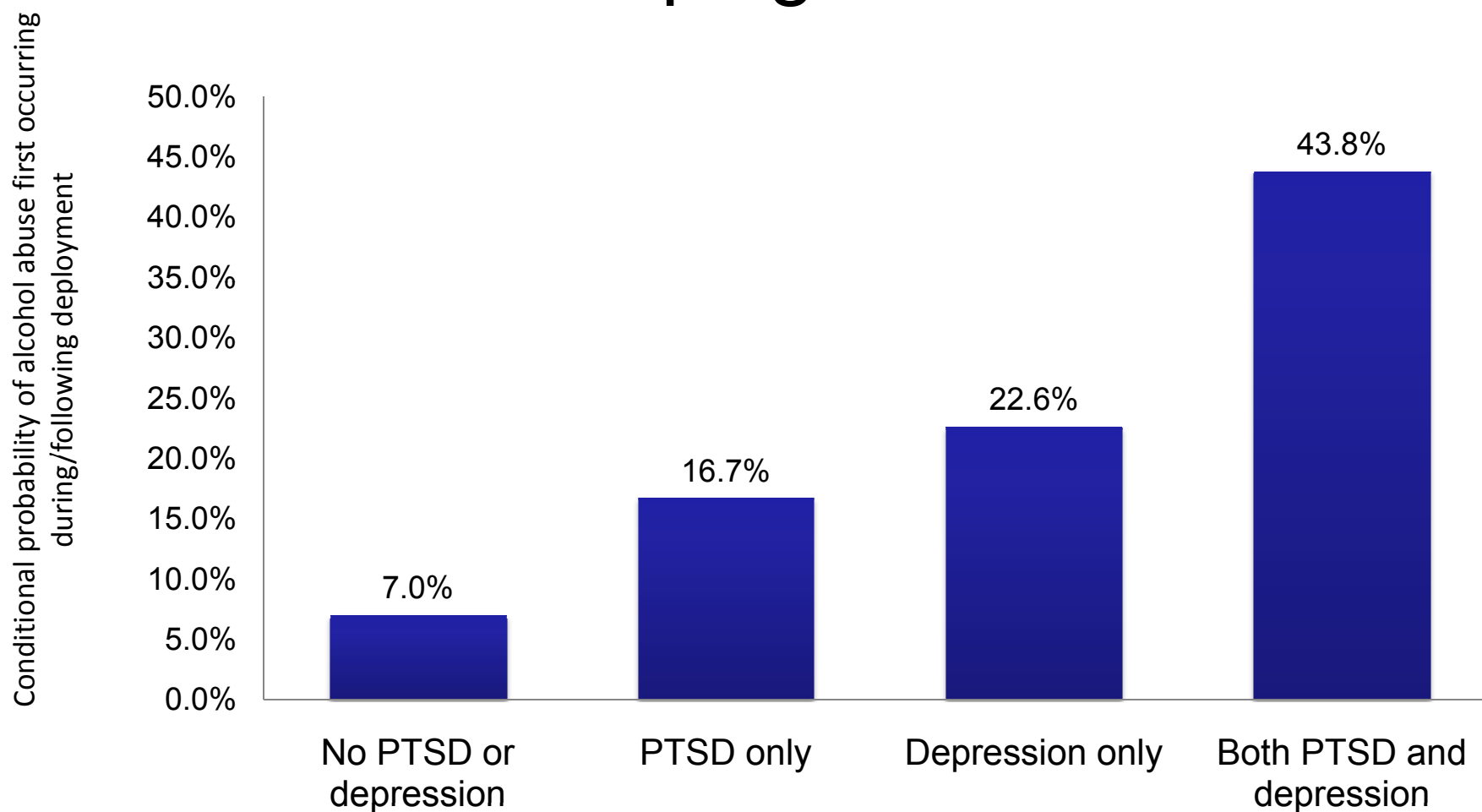
Alcohol Dependence, Current Depression, and Suicidal Ideation

30

Both Alcohol Dependence & Current Depression Independently Associated with Suicidal Ideation
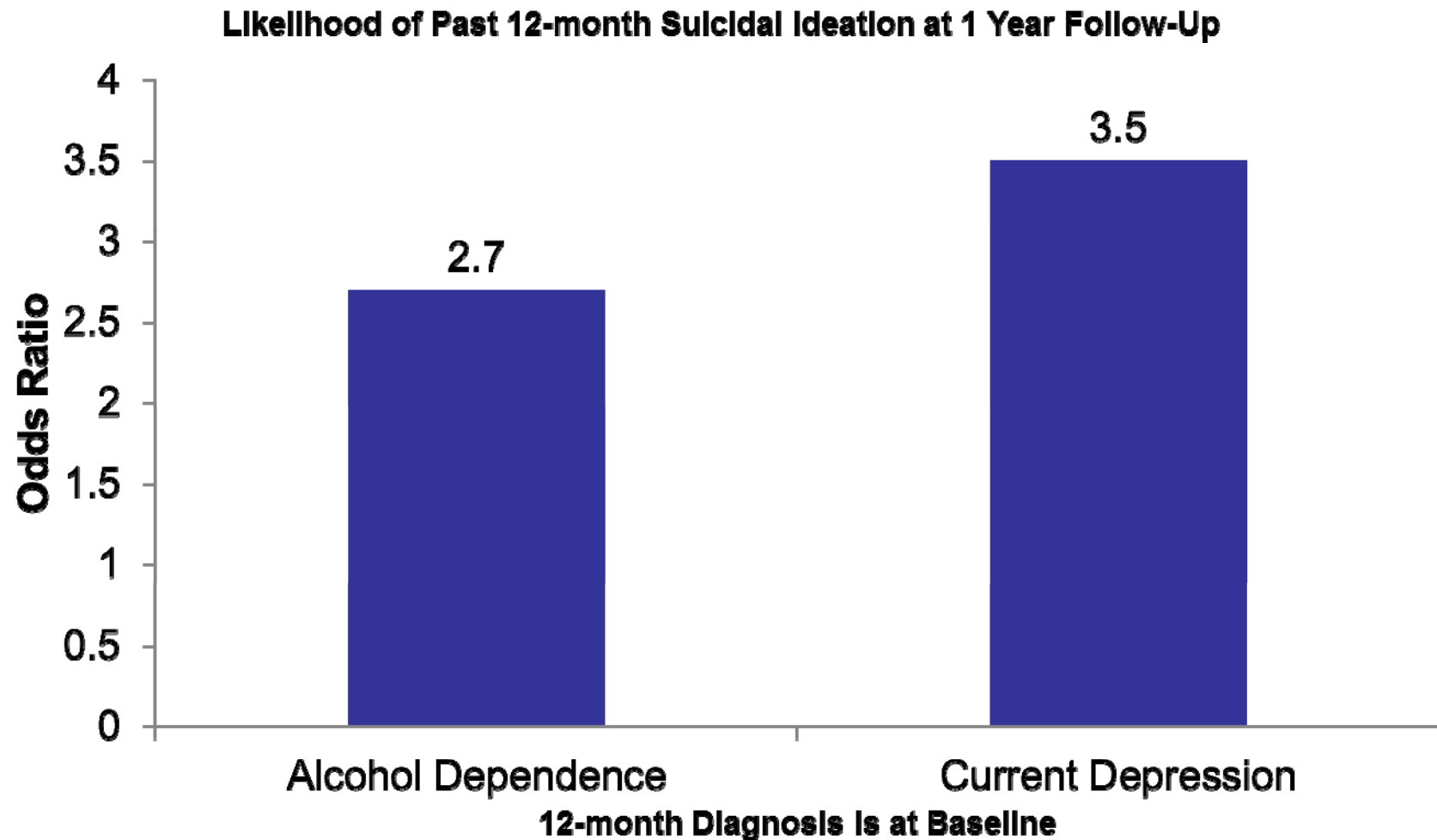
Likelihood of Past 12-month Suicidal Ideation at 1 Year Follow-Up

Cohen, G.H., Prescott, M. R., Liberzon, I., Tamburrino, M. B., Calabrese, J. R., & Galea, S. (Under Preparation). Alcohol Dependence and Incident Suicidal Ideation

31

PTSD and Depression Increases the Risk of Developing Alcohol Abuse

Conditional probability of alcohol abuse first occurring during/following deployment

- No PTSD or depression: 7.0%
- PTSD only: 16.7%
- Depression only: 22.6%
- Both PTSD and depression: 43.8%

Presence of mental health conditions first occurring during/following deployment

32

Marshall BDL et al. Coincident posttraumatic stress disorder and depression predict alcohol abuse during and after deployment among Army National Guard soldiers. *Drug and Alcohol Dependence* 2012; 124: 193-199.

HIV-Risk Taking Behavior

# Past year HIV risk behavior is associated with PTSD, depression, and history of alcohol use disorder

PTSD*
- yes: 14
- no: 6

Depression*
- yes: 11
- no: 5

AUD history *
- yes: 21
- no: 6

% with past year HIV risk behavior
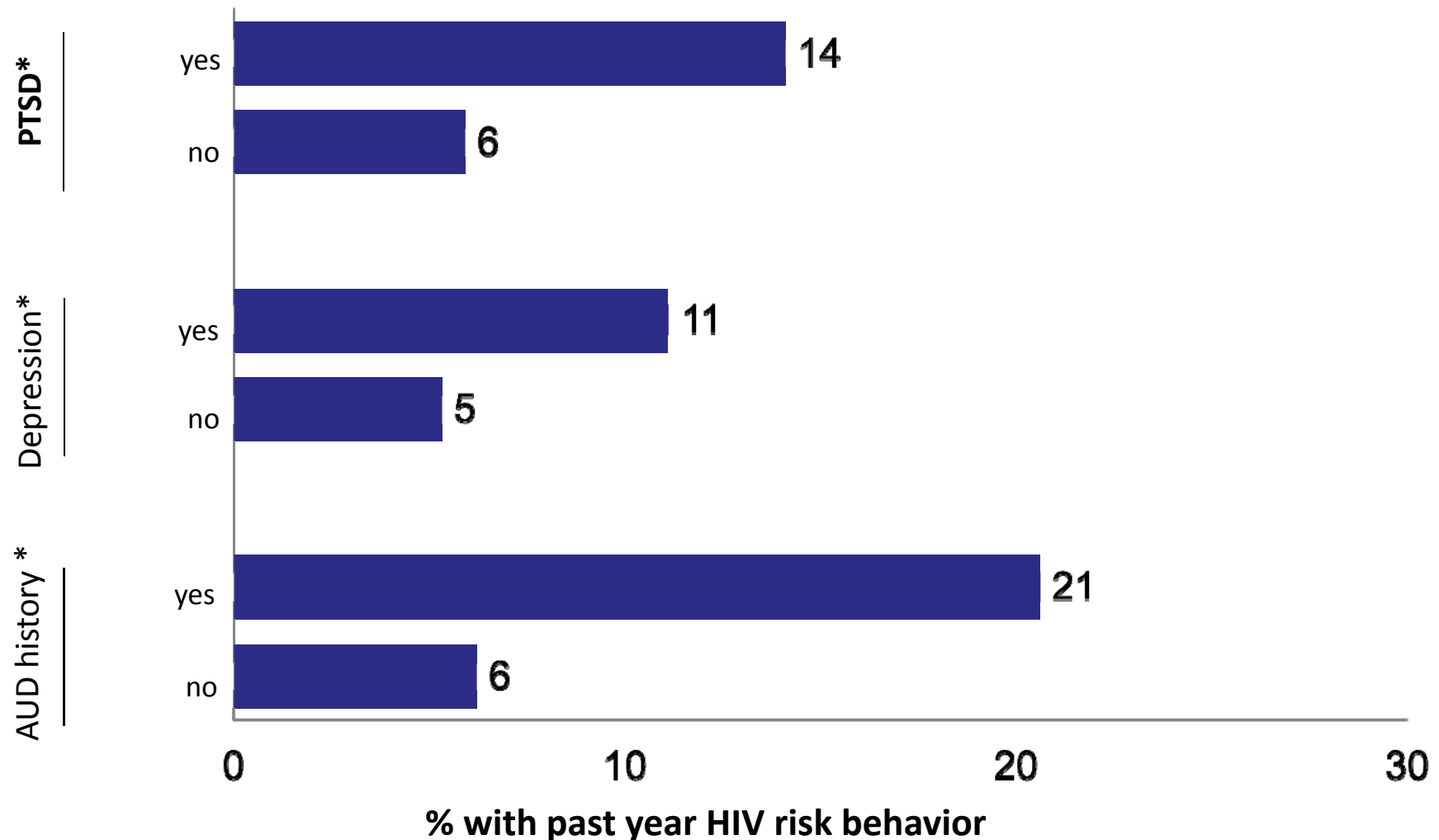
*n=2282; all comparisons significant at p<0.01; AUD = alcohol use disorder, including abuse and dependence

Marshall B, Prescott M, Liberzon I, ... Galea S: PTSD, Depression, and HIV Risk Behavior Among Ohio Army National Guard Soldiers. *Journal Traumatic Stress*, 2013;*26*(1): 64-70. [34]

Cigarette Smoking and Suicidal Ideation

Smoking at baseline doubles the risk of suicidal ideation at one year follow-up (3% vs. 6%)

Smoked at baseline

Suicidal ideation at follow-up

Yes 31%

Suicidal ideation at follow-up

Yes 6%

No 94%

No 69%

Yes 3%

No 97%
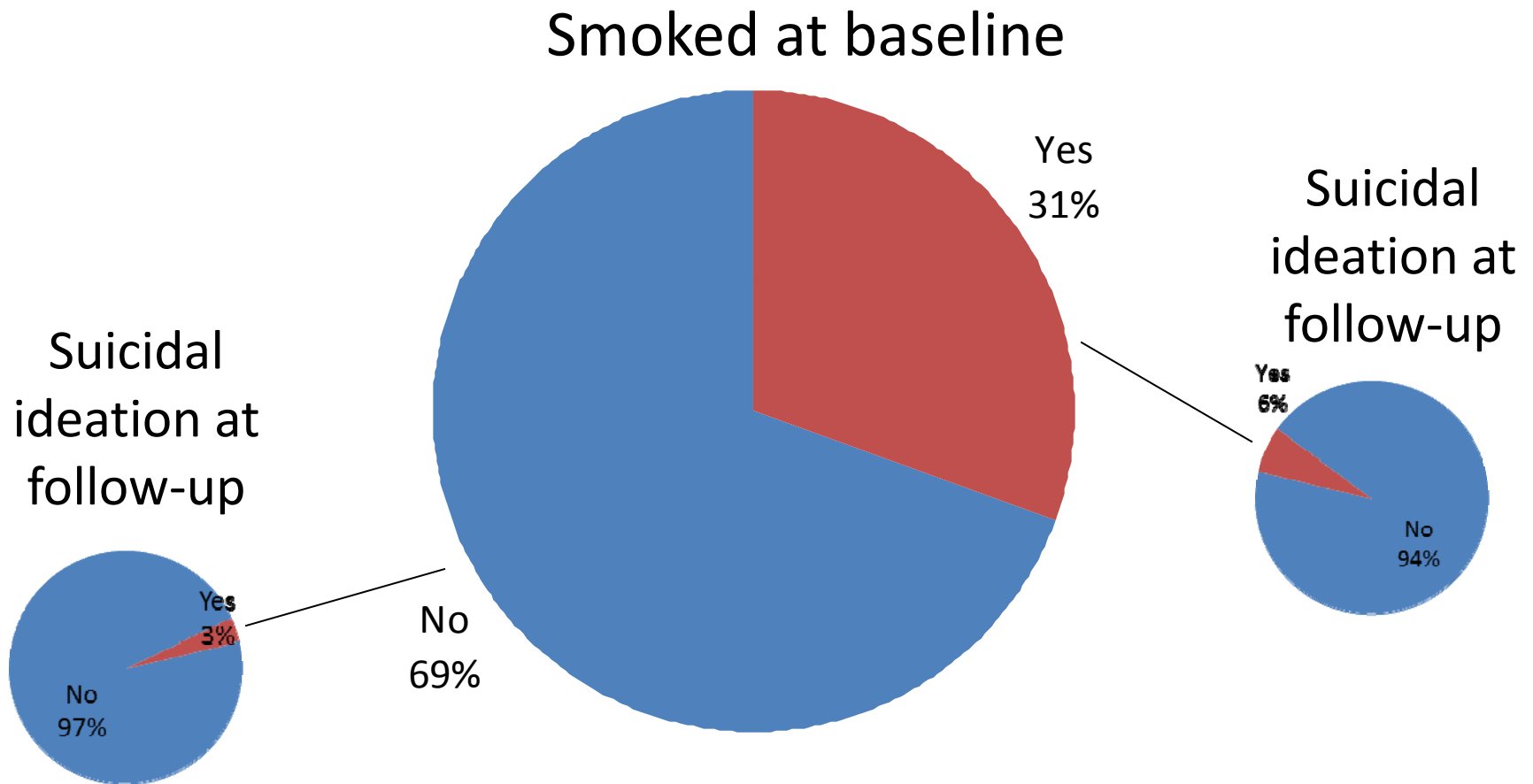
Goodwin R, Prescott M, Tamburrino M, … Galea, S. Cigarette smoking and subsequent risk of suicidal ideation among National Guard Soldiers. *Journal Affect. Dis.*. In Press. 2012.

Longitudinal sample at wave 2; n=1766.

Cigarette Smoking and Depression

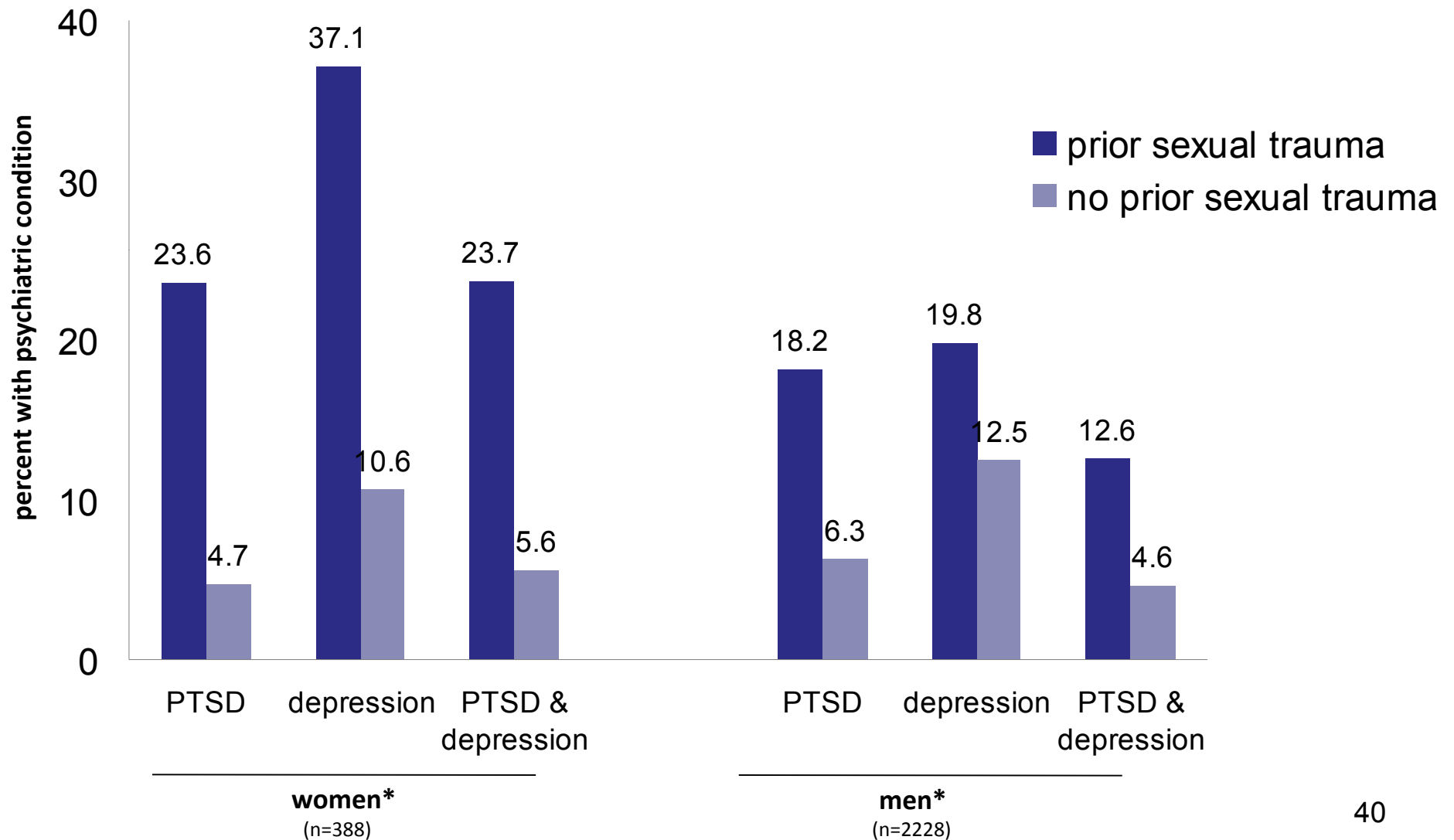# Only chronic smokers are twice as likely to develop incident depression
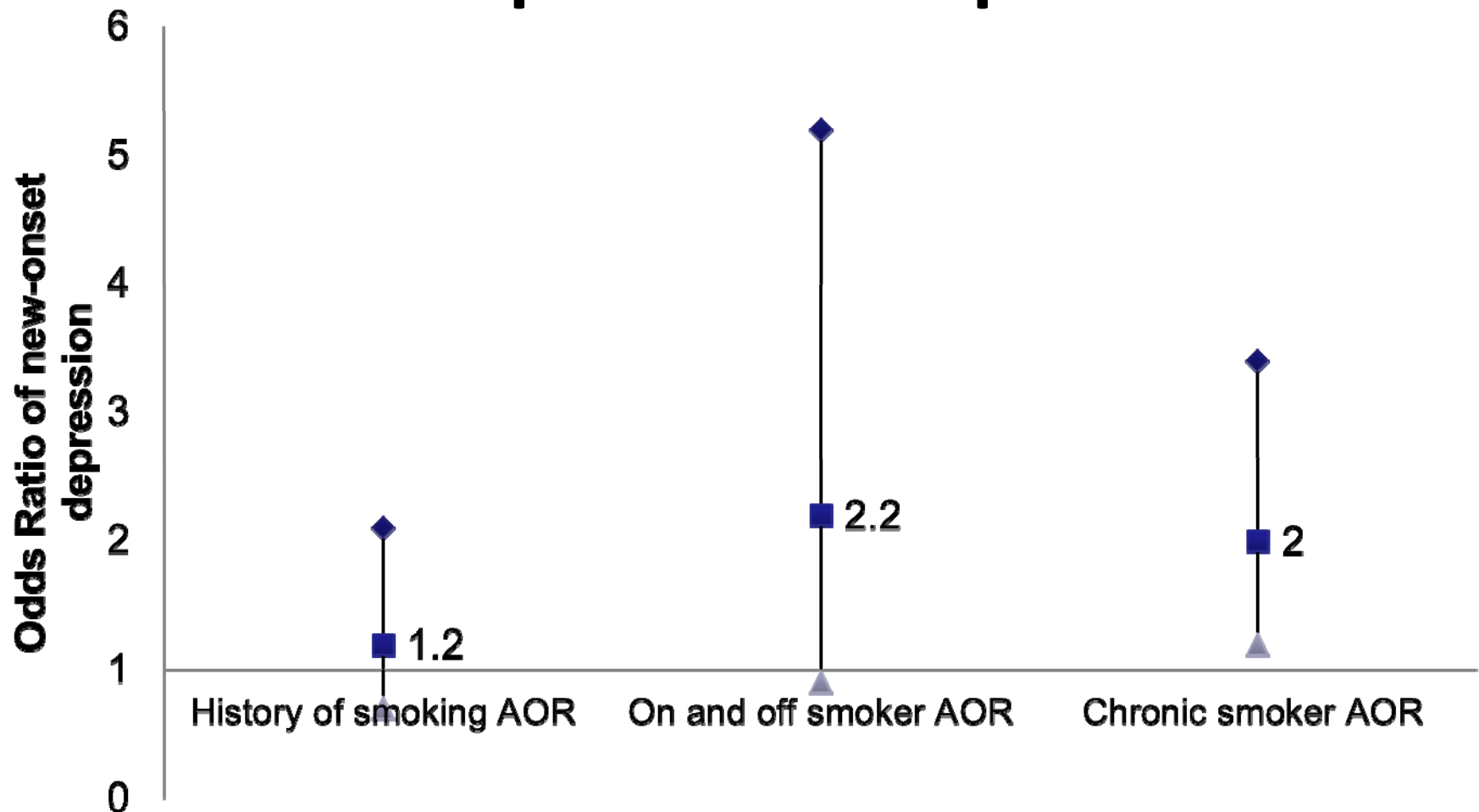
*Model is adjusted for age and gender, AOR = Adjusted Odds Ratio

Goodwin R, Prescott M, Tamburrino M, Calabrese J, Liberzon I, Galea S: Does smoking predict depression onset among military personnel?. *Psychiatry Research*. In Press. 2012
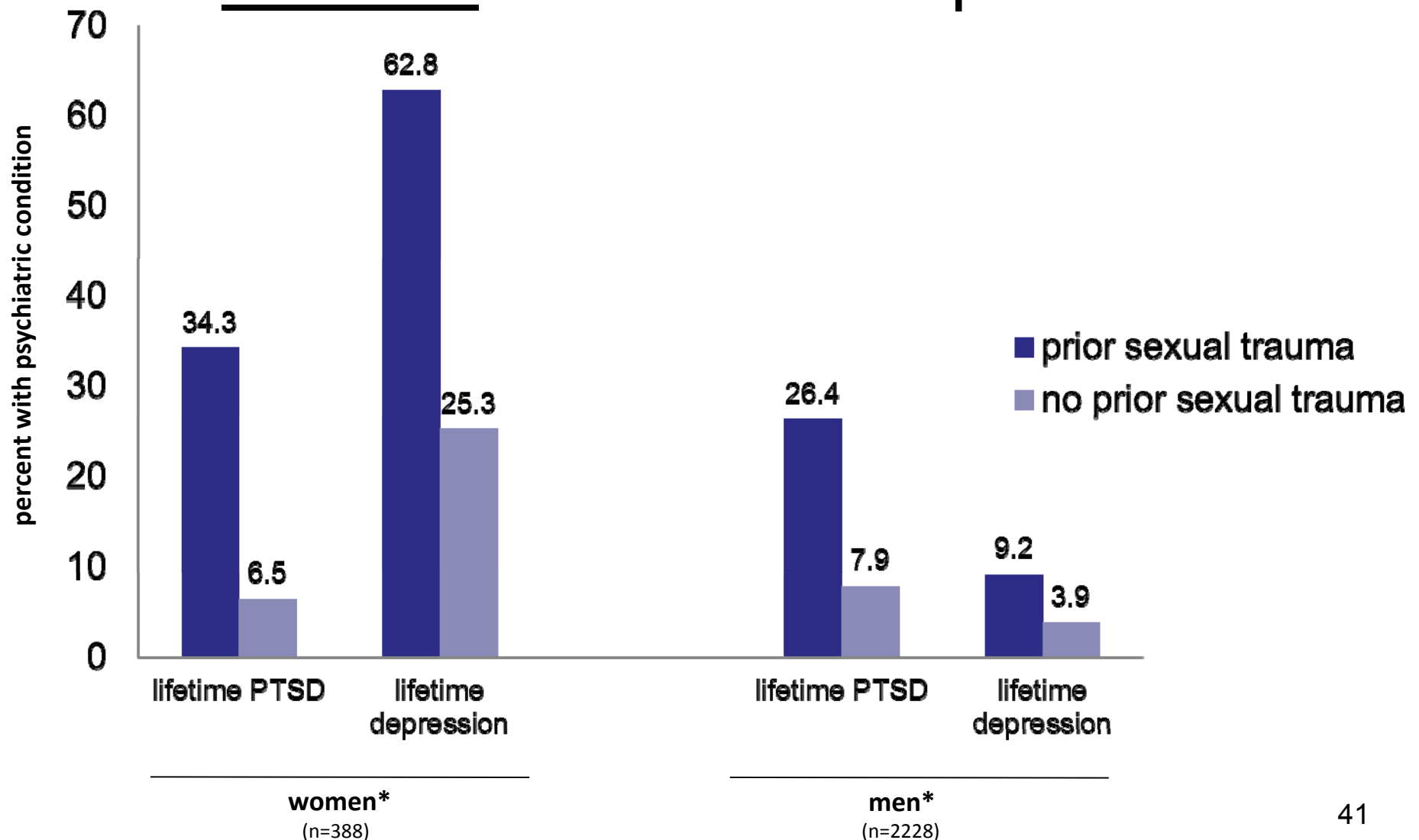
Prior Sexual Trauma, PTSD, and Depression

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Prior Sexual Trauma is Associated with <u>Past year</u> PTSD and Depression

prior sexual trauma
no prior sexual trauma

percent with psychiatric condition

women* (n=388)

men* (n=2228)

PTSD: 23.6, 4.7
depression: 37.1, 10.6
PTSD & depression: 23.7, 5.6

PTSD: 18.2, 6.3
depression: 19.8, 12.5
PTSD & depression: 12.6, 4.6

n=2616; *all comparisons significant at p<0.001

Walsh, K et al. Sexual Violence and Mental Disorders Among National Guard and Reserve Soldiers. (Under Review). 2012. American Journal of Public Health

40

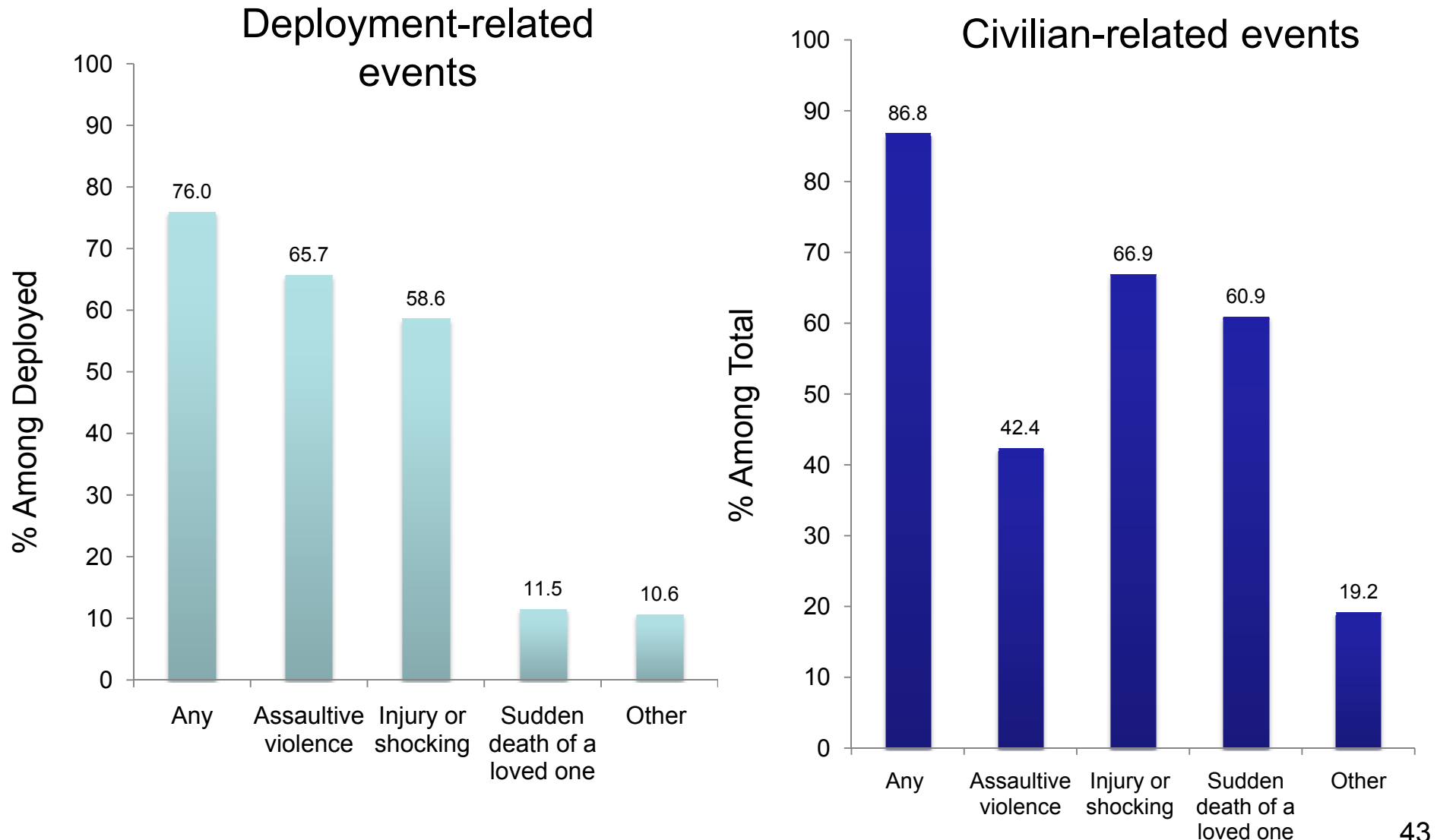# Prior Sexual Trauma is Associated with <u>Lifetime</u> PTSD and Depression


n=2616; *all comparisons significant at p<0.001

Walsh, K et al. Sexual Violence and Mental Disorders Among National Guard and Reserve Soldiers. (Under Review). 2012. American Journal of Public Health

41

TRAUMA EXPOSURE

42

Trauma exposure is comparable in military and civilian settings

Deployment-related events

% Among Deployed

- Any: 76.0
- Assaultive violence: 65.7
- Injury or shocking: 58.6
- Sudden death of a loved one: 11.5
- Other: 10.6

Civilian-related events

% Among Total

- Any: 86.8
- Assaultive violence: 42.4
- Injury or shocking: 66.9
- Sudden death of a loved one: 60.9
- Other: 19.2

43

n deployed at baseline = 1668, n total at baseline = 2616

Participants experienced more civilian traumas

- Most soldiers experienced ≥ 1 type of traumatic event in a civilian setting.

- 1/3 experienced both military and civilian traumas

- ~90% had experienced at least one lifetime traumatic event, and of those, over half reported at least one assaultive event

Military and Civilian traumatic events 29%

No traumatic events 12%

Military traumatic events only 9%

Civilian traumatic events only 50%
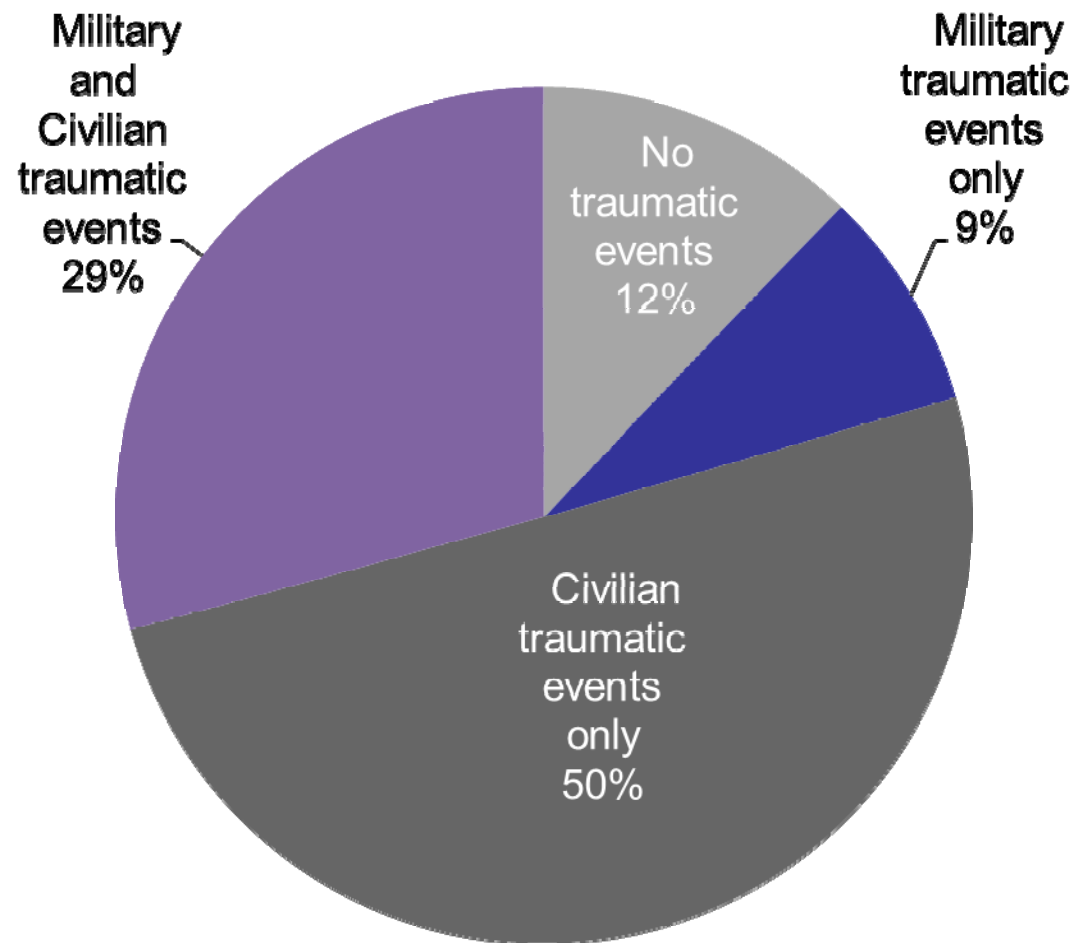
n = 1839, respondents in baseline who specified their deployment status and did not have events of ambiguous settings or types

44

12-month depression outcomes differ by type of trauma
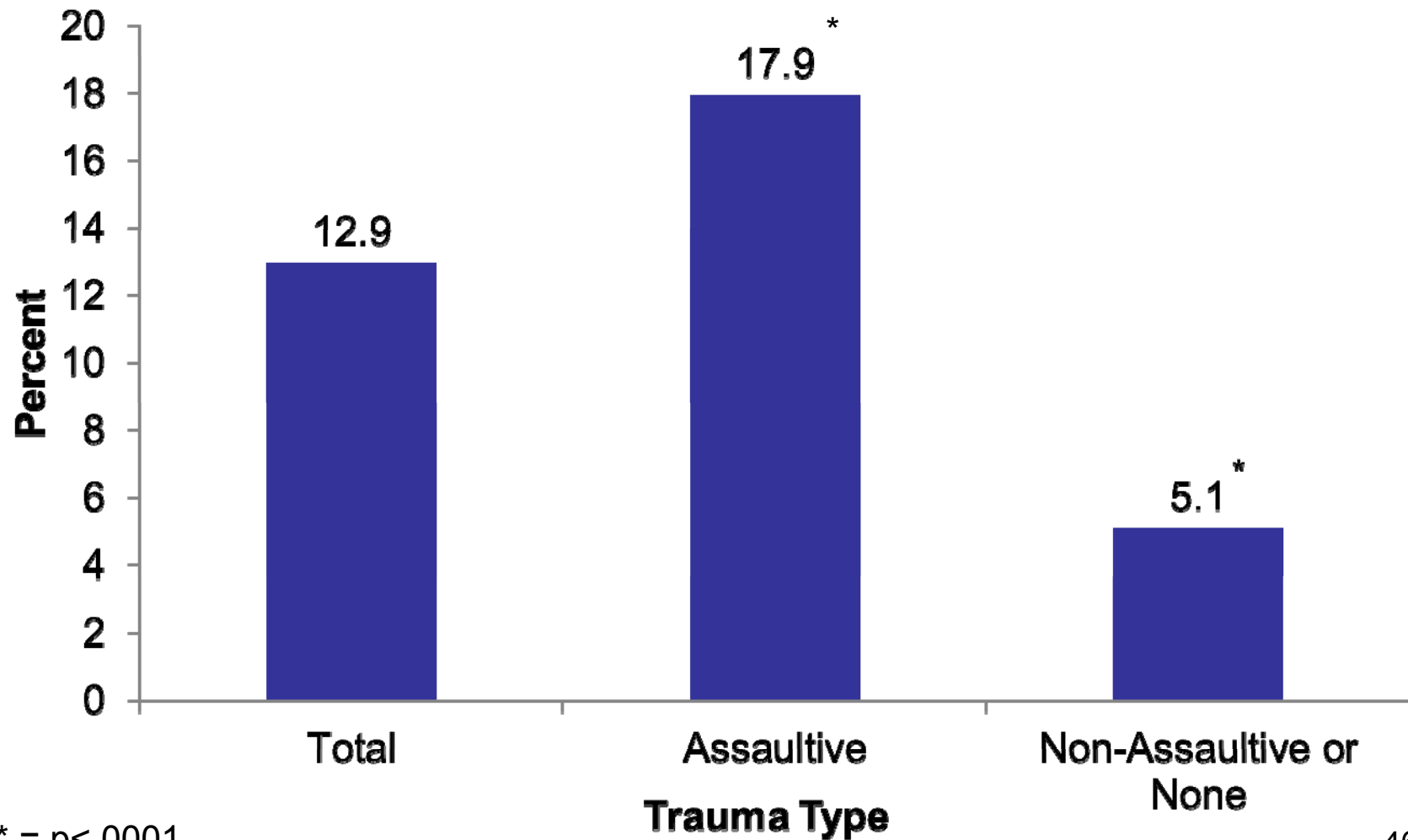
Percent

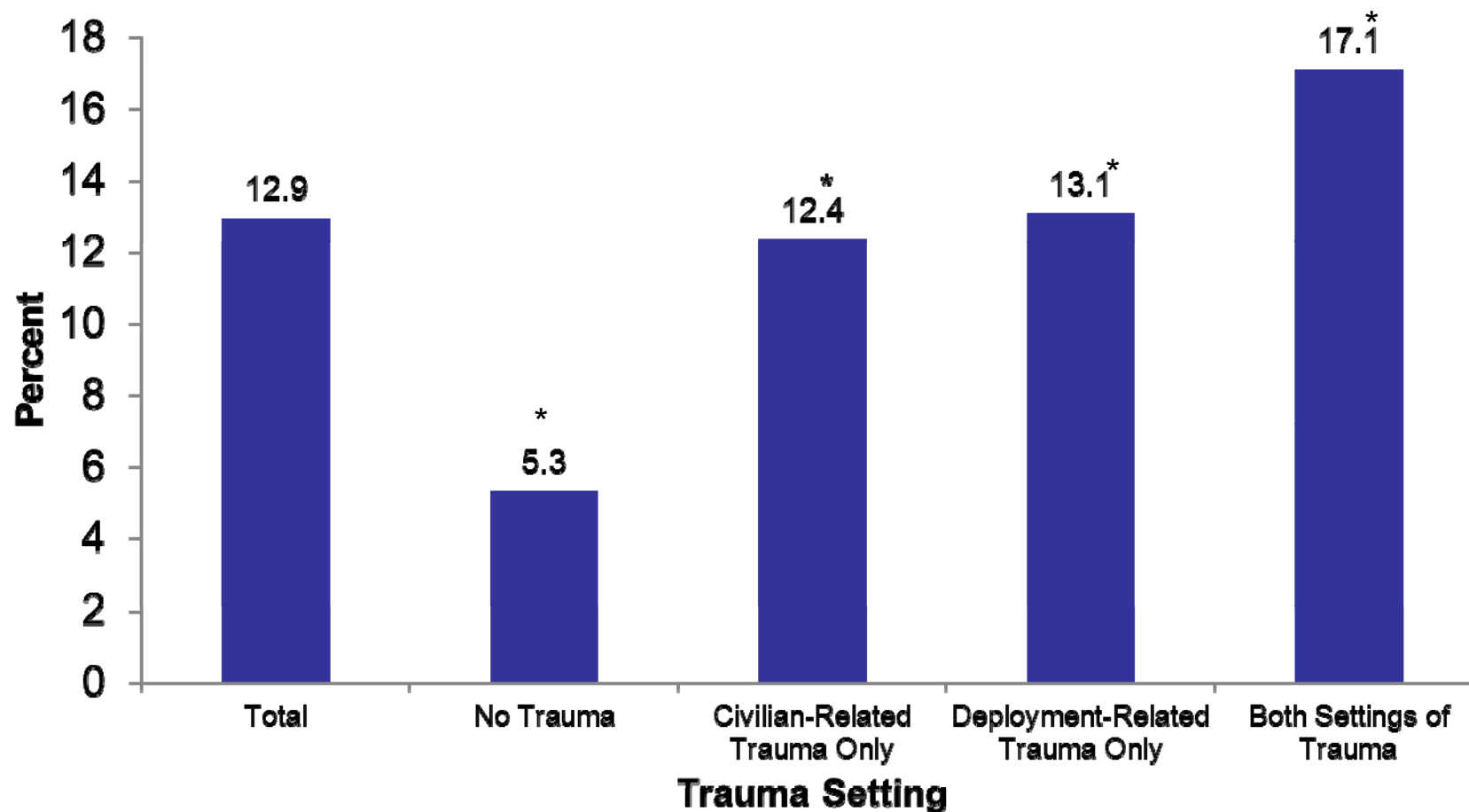|	Total	Assaultive	Non-Assaultive or None
	12.9	17.9 *	5.1 *

Trauma Type

* = p<.0001
Includes respondents in baseline who specified their deployment status and did not have events of ambiguous settings or types

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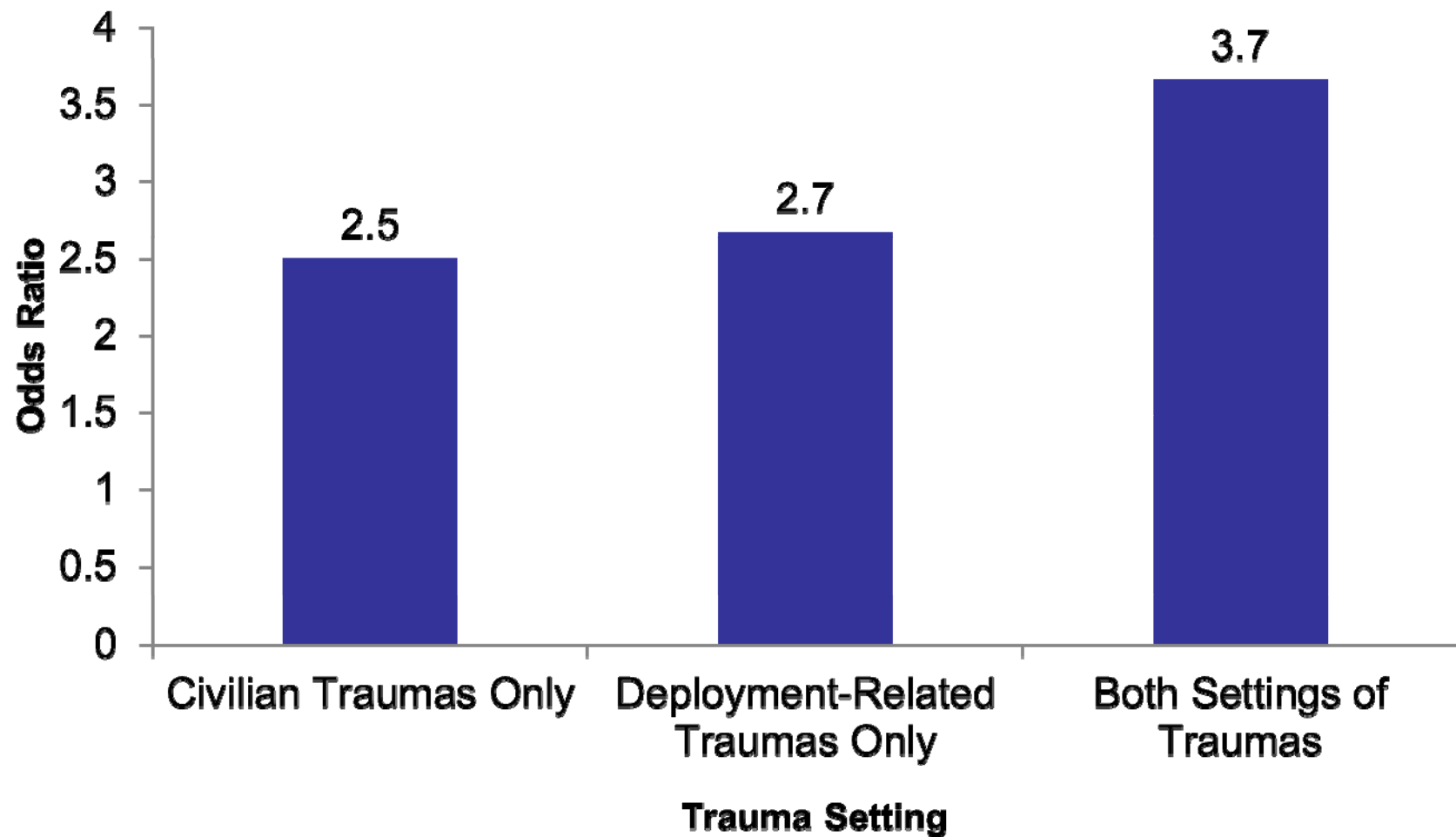# 12-month depression outcomes differ by setting of trauma

* = p<.0001

Includes respondents in baseline who specified their deployment status and did not have events of ambiguous settings or types
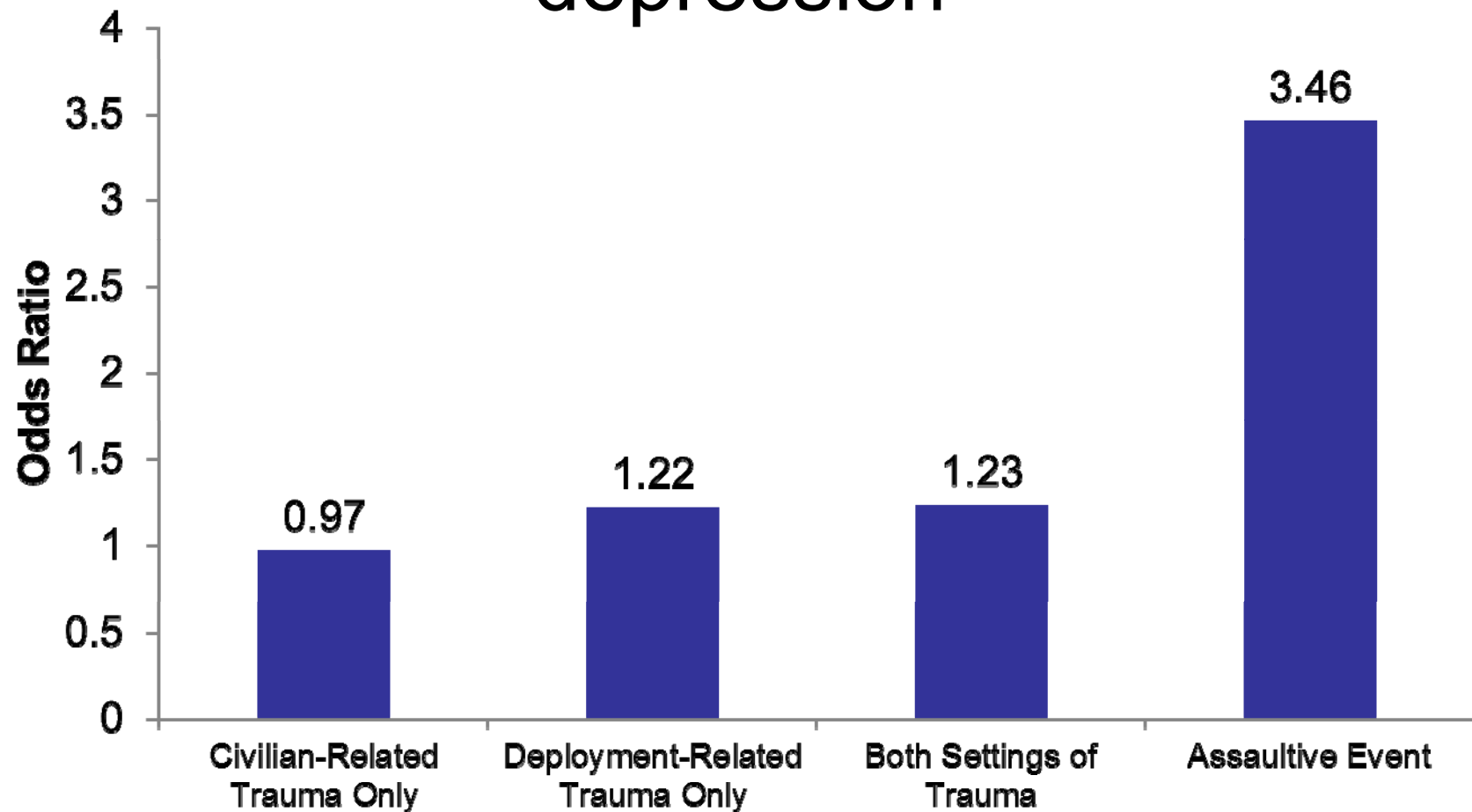
Dose response relationships observed in setting of trauma predicting 12-month depression

N = 1839: Includes respondents in baseline who specified their deployment status and did not have events of ambiguous settings or types
Comparison Group: No Traumas

48

Type of event is more important than setting of event in predicting 12-month depression

Potential Role of Personalized Training at the Time of Enlistment?

50

TRAJECTORIES vs. Potentially Misleading Cumulative Prevalence Rates

# Majority resistant to the development of PTSD symptoms over 2 years

- 93.7% of respondents with a potentially traumatic event were resistant to PTSD

- 5% with a potentially traumatic event showed a recovery from moderate to mild symptoms

- 1.3% with a potentially traumatic event showed chronic dysfunction
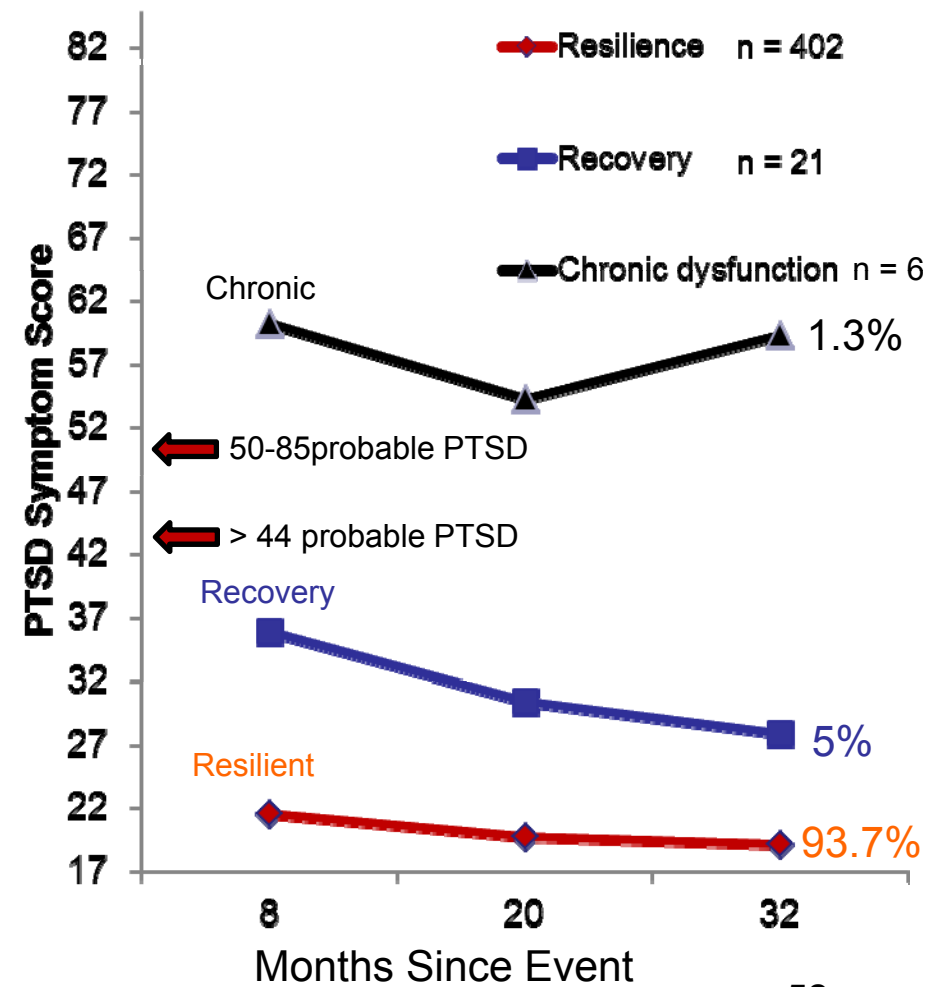
PTSD Sx severity: 44 = probable PTSD; 50-85 definite PTSD;
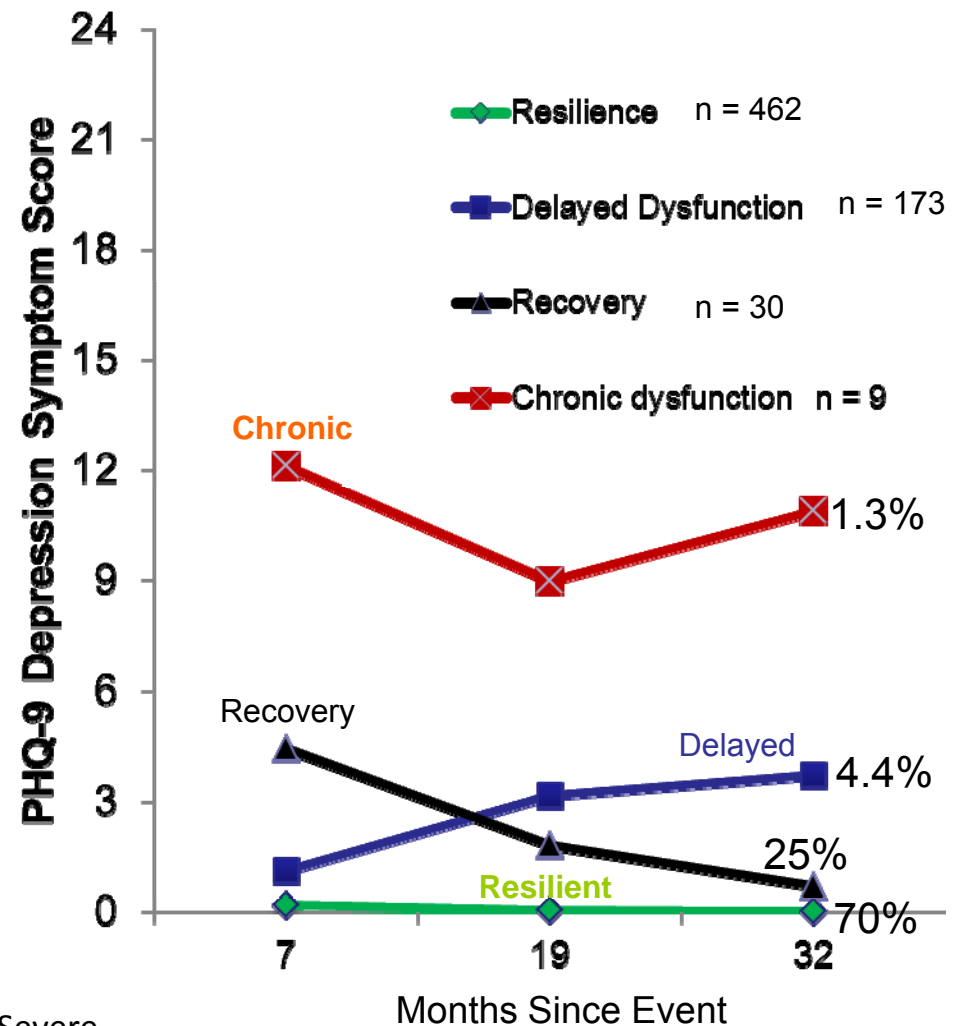*n=429, participants who completed at least 2 waves of the study, had a traumatic event during a deployment within 2 years of baseline assessment, and were bothered by the same event throughout the follow-up interviews.

Lifetime prevalence of PTSD over 3 years

Telephone Survey Sample: N = 1164. Alcohol Use Disorder = alcohol abuse and alcohol dependence.
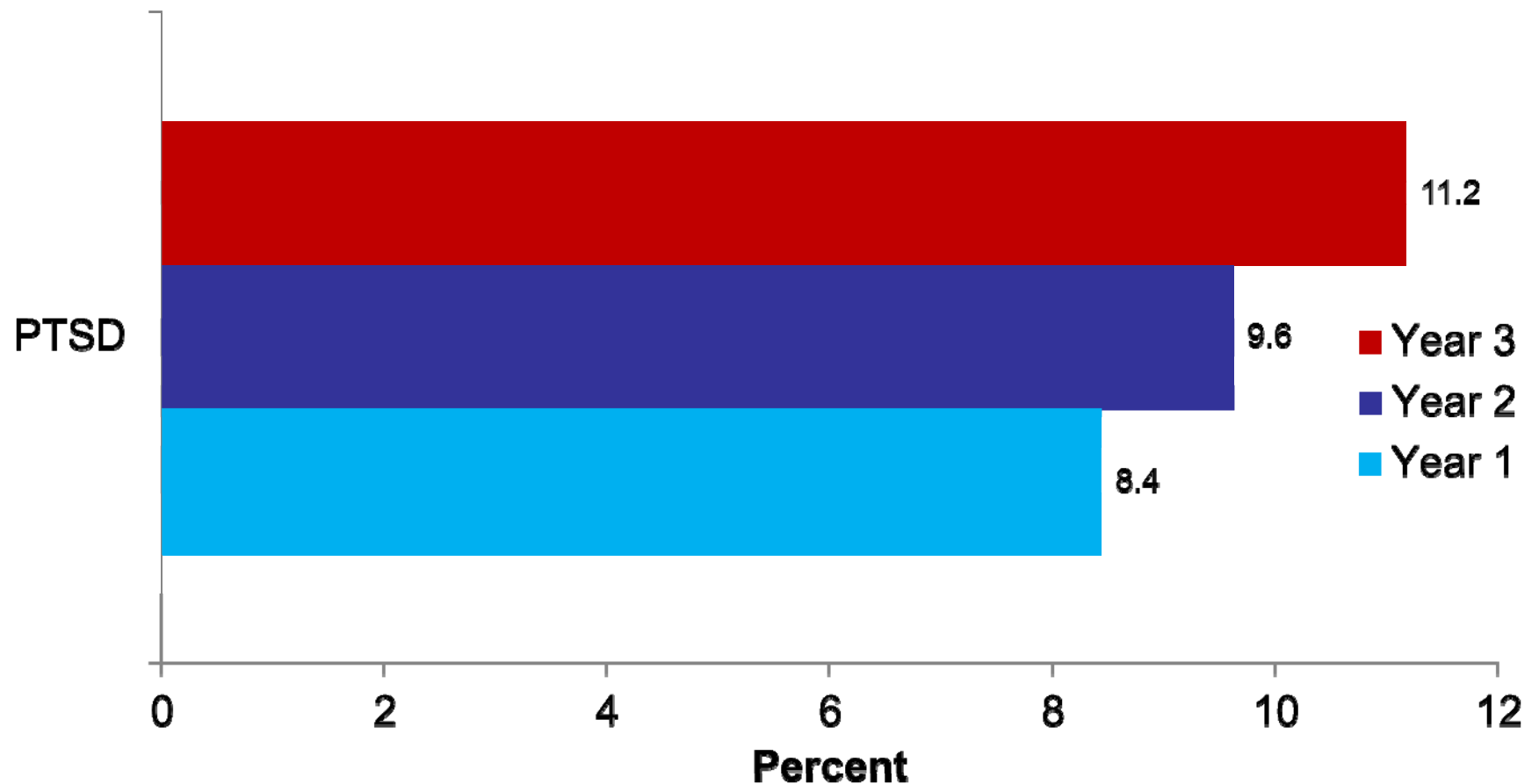
Following deployment most were resistant to depression symptoms over 2 years

- ~70% were resistant to depression symptoms following deployment

- Following deployment, about 1/4 of respondents showed recovery from mild to no symptoms.

- 4.4% displayed possible delayed dysfunction, going from a low symptom score to a mild severity

- 1.3% showed chronic dysfunction, reporting most symptoms at least several days in the past 30

5, 10, 15, and 20 = Mild, Moderate, Moderately Severe, and Severe.

*n=674, participants who completed at least 2 waves of study and deployed within 2 years of the baseline assessment.

Lifetime prevalence of depression over 3 years
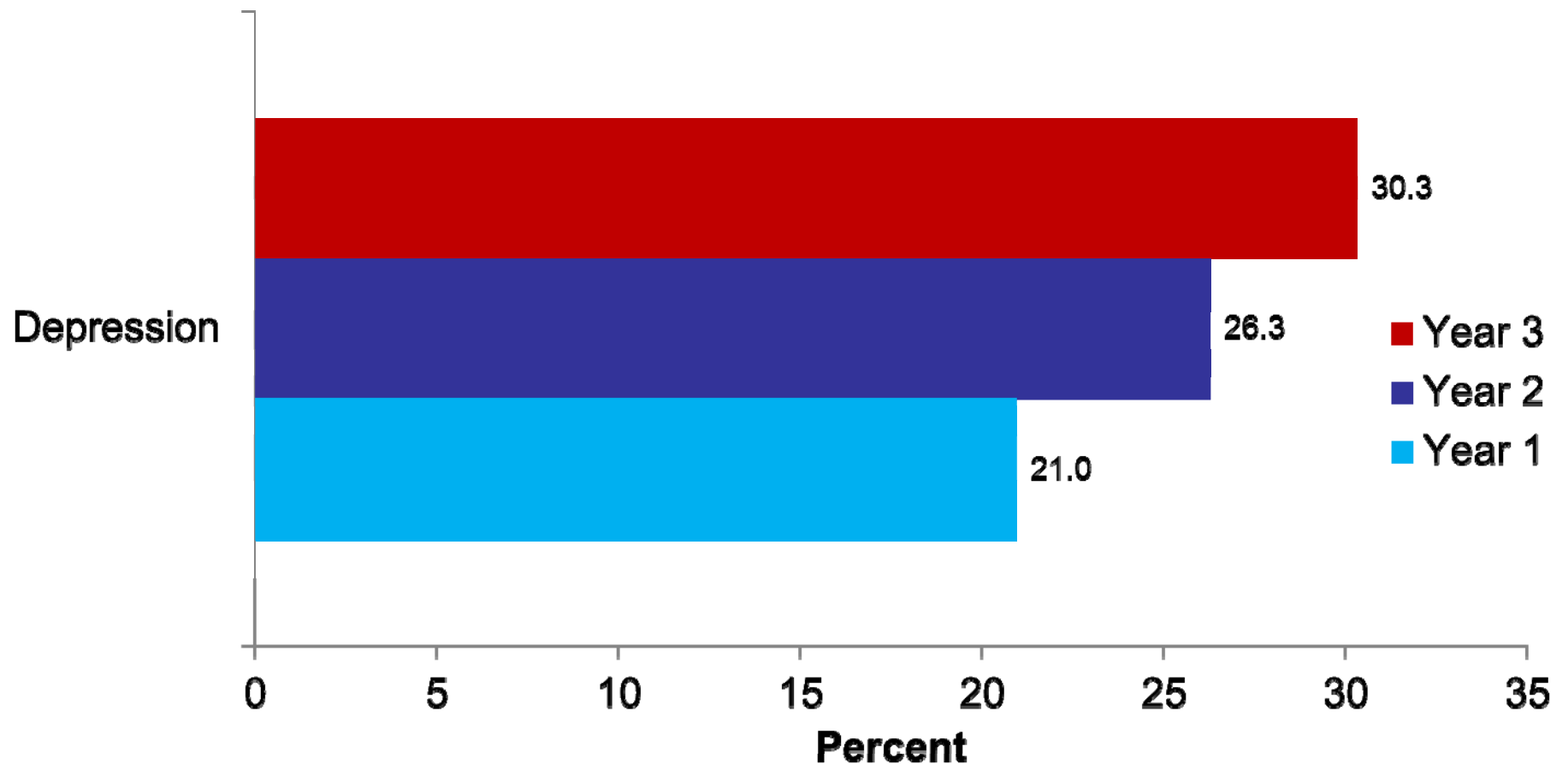
Telephone Survey Sample: N = 1164. Alcohol Use Disorder = alcohol abuse and alcohol dependence.

Findings, implications, and conclusions

Overall rates of 5 illnesses studied were not remarkably increased.

However, vulnerable subgroups do exist within the Ohio Army National Guard

To serve and protect the force and families, vulnerable subgroups would probably benefit from personalized pre-deployment training.

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Future Directions

- Direction provided by COL Castro (Director, Military Operational Medicine Research Program) and the advisory board on February 19, 2013 Fort Detrick

  1. Expand the focus to include general physical and emotional health.

  2. Duplicate the Ohio platform in other geographically and ethnically diverse states.

Publications

Title	First Author	Year
PTSD comorbidity and suicidal ideation associated with PTSD within the Ohio Army National Guard – **Journal of Clinical Psychiatry**	**Joseph R. Calabrese, MD**	**2011**
Potentially Modifiable Pre-, Peri-, and Post-deployment Characteristics Associated With Deployment-Related Posttraumatic Stress Disorder Among Ohio Army National Guard Soldiers - **Annals of Epidemiology**	**Emily Goldmann, PhD**	**2011**
Coincident posttraumatic stress disorder and depression predict alcohol abuse during and after deployment among Army National Guard soldiers – **Drug and Alcohol**	**Brandon D. Marshall, PhD**	**2011**
The factor structure of major depression symptoms: A test of four competing models using the Patient Health Questionnaire-9 – **Psychiatry Research**	**Jon D. Elhai, PhD**	**2012**
Posttraumatic stress disorder and HIV risk behavior among Army National Guard soldiers: The mediating role of depression. – **Journal of Traumatic Stress**	**Brandon D. Marshall, PhD**	**2012**
Cigarette smoking and subsequent risk of suicidal ideation among National Guard Soldiers – **Journal of Affective Disorders**	**Renee D. Goodwin, PhD**	**2012**
Does smoking predict depression onset among military personnel? – **Psychiatry Research**	**Renee D. Goodwin, PhD**	**2012**
Relations between the underlying dimensions of PTSD and major depression using an epidemiological survey of deployed Ohio National Guard soldiers – **Journal of Affective Disorders**	**Tracy L. Biehn**	**2012**
Validation of lay-administered mental health assessments in a large Army National Guard cohort – **International Journal of Methods in Psychiatric Research**	**Marta R. Prescott, PhD**	**2013**

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Genetic Studies of PTSD in Ohio National Guard Soldiers Deployed to Iraq and Afghanistan: Replication of G x E interaction in FKBP5 and 5-HTTLPR

Category: Genetic: humans

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Background: Posttraumatic stress disorder (PTSD) is a chronic, debilitating disease that leads to substantial human suffering and costs to society. Military deployment and exposures to combat trauma are associated with high incidence of PTSD, estimates of up to 1 in 5 US soldiers and Marines deployed to Iraq developed clinically significant symptoms of PTSD. Twin and family studies suggest that PTSD is heritable, with estimates of up to 40% of variance in PTSD symptoms explained by genetic factors. Molecular genetic studies of candidate genes in trauma-exposed populations has not found "main effects" of gene association with PTSD, but rather have suggested gene x environment (G x E) interaction, (including gene x childhood adversity interactions), in the serotonin transporter (*SLC6A4*), *FKBP5* and *RGS2* genes, but these have not been replicated.

Methods: A random sample of 2616 Ohio Army National Guard (ONG) soldiers was recruited, and   structured telephone interviews were conducted at three time points (pre- and post-deployment, "Waves" 1-3) to assess deployment-related and lifetime traumatic event exposure, including childhood abuse and adversity, and DSM-IV criteria PTSD (interview adapted from PTSD Checklist, PCL). Deployments included Afghanistan (OEF), Iraq (OIF), and other operations. Additional psychiatric symptoms were obtained using validated instruments, and other data using multi-measure scales adapted from the Deployment Risk and Resilience Survey. Soldiers were requested on Wave 2 interview to consent to provide saliva specimens and additional self-report measures, collection kits (Oragene) were sent to participant's homes and shipped to our lab by return mail. Genomic DNA was purified using a semi-automated filter-based system. Genotyping was performed using PCR (serotonin transporter gene (*SLC6A4*) 5-HTTLPR, *DRD4* VNTR), and a custom 4800 SNP Illumina array. This array maps ~120 candidate genes and genomic regions previously identified in candidate or GWAS studies of other psychiatric disorders, and includes *FKBP5*, *RGS2*, and *CRHR1* genes previously implicated in PTSD, as well as ancestry informative markers. Standard Illumina clustering and data cleaning was performed, data pruning generated 1500 markers in

equilibrium for principal component analyses to control for population substructure. Association of previously reported variants with level of PTSD symptoms was tested in GLM modeling of main effects of gene (SNP), controlling for levels of childhood abuse (0, 1, or 2 or more types), and lifetime trauma load (ordinal 1-4 levels), and also including gene x child abuse and gene x trauma load interaction terms.

Results: The majority of soldiers (80%) agreed to be sent a genetic specimen collection kit, and 1042 returned genetic specimens and self-report data (50% return rate). 136 participants did not endorse any lifetime trauma, and were excluded from further analyses. The highest of the available PCL scores was used for association analyses (available data N = 766). As expected, PCL score was associated with report of child abuse (F[2,754] = 12.4. p <.00001) and lifetime trauma load (F[3,753] = 14.9. p <.00001). Four SNPs in *FKBP5* (rs1360780, rs3800373, rs9296158, rs9470080) all showed SNP x child abuse interactions (all p < .007), but no main effect on PCL. The triallelic 5-HTTLPR also showed gene x child abuse interaction in a recessive model (p < .005), but no main effects. *RGS2*, *DRD4*, and *CRHR1* all showed no main effects and no interaction effects for association with PCL.

Conclusions: To our knowledge, this is the first report of genetic association with PTSD symptoms in soldiers deployed to Iraq and Afghanistan. We have replicated previous findings of G x E interaction effects in *FKBP5* and 5-HTTLPR in this cohort. Further analyses are ongoing to identify additional genetic variants associated with PTSD.

Keywords: PTSD, genetics, gene x environment interaction, military, combat trauma

Abstract for Case ShowCase Poster

Title: Unit Cohesion among Deployed Soldiers and Alcohol Use Disorders

Objective: To evaluate the impact of Unit Cohesion in deployed soldiers and alcohol use disorders.

Methods: 1052 (40.2%) of 2616 OHARNG soldiers who completed a telephone survey were randomly invited for an in-depth clinical assessment using the Structured Clinical Interview for DSM-IV-TR (SCID) and the Clinician-Administered PTSD Scale (CAPS). Of the 1052 invited, 500 in-depth clinical interviews were conducted in neutral settings across Ohio, in 2008 and 2009. Of the 500 in-depth clinical interviews, 337 were eligible for the following analyses. The study data also included demographic variables as well as data from the Deployment Risk and Resilience Inventory (DRRI). All models were adjusted for age, gender, and race.

Results: A lifetime diagnosis of alcohol use disorder was present in 53.1% of the study sample. The odds of a lifetime diagnosis of alcohol use disorder decreased as the scores on deployment social support increased (OR = 0.996, 95% CI= 0.96-1.03). The odds also decreased in the development of current alcohol abuse as the scores on the deployment social support increased (OR = 0.981, 95% CI= 0.89-1.08). The odds of a current diagnosis of alcohol dependence increased as the scores on the deployment social support increased (OR=1.13, 95% CI = 0.998-1.28). The total score of the deployment social support subscale was not statistically significant in predicting alcohol use disorders.

Conclusion: The results suggest that soldiers who have greater unit support are less likely to develop a lifetime alcohol use disorder or current alcohol abuse, but not current alcohol dependence. Further study is necessary to understand the complexity of unit support on alcohol use disorders.

Abstract for Spirituality Case Showcase Poster

Title: Does spirituality predict suicidal ideation or behavior? Results from an analysis of Ohio Army National Guard soldiers.

Objective: To evaluate the impact of spiritual well-being, either as religious or secular (existential), on suicidal ideation and behavior.

Methods: A population-based sample of 418 Ohio Army National Guard (OHARNG) soldiers was analyzed from data obtained from an in-person, clinician-conducted survey. The survey data included demographic variables, results from a 21 item Spirituality Well-Being Survey (SWBS) assessment, a 15 item Columbia Suicide Self-Report (CSSR) scale and 28 item Childhood Trauma Questionnaire (CTQ). The SWBS provided both a religious and existential measure of spiritual well-being as well as an overall spiritual measure. Scores on the SWBS were treated as continuous variables in logistic regression models of suicidal ideation and suicidal behavior assessed by the CSSR. Higher scores indicate a more positive feeling of well-being. Models were adjusted for age, gender, race and emotional/physical/sexual abuse as a child (rated via the CTQ).

Results: Suicidal ideation occurred in 32/418 = 7.7% of the soldiers. The odds decreased as their scores on spiritual well-being and existential well-being increased (OR = 0.97, 95% CI 0.95-0.99 for spiritual and OR = 0.93, 95% CI 0.89-0.97 for existential). Suicidal ideation was not statistically significantly influenced by religious well-being (OR = 0.98, 95% CI 0.95-1.01). None of the spirituality scores affected suicidal behavior which presented in 37/418 = 8.9% of the soldiers. Presence of childhood emotional abuse indicated a greater risk of suicidal ideation, but not suicidal behavior, in all of the models.

Conclusions: These results suggest that soldiers who have a more positive outlook on life, regardless of religious beliefs, are less likely to experience suicidal ideation than those with a less positive outlook.

Mining Associations between Traumatic Events and Psychiatric Diagnoses in the Ohio Army National Guard Mental Health Initiative

Background: Association rule mining algorithms are regarded as reliable techniques in inducing the rules that govern the data; since the introduction of the Apriori algorithm; the first association rule algorithm (1); many algorithms have emerged in the computer science literature. This work aims to utilize the HotSpot algorithm (2) implemented in Weka researching to discover association rules between different traumatic events, pre-diagnostic screening questions for psychiatric disorders in the SCID, the alcohol use and depression modules of the OHARNG-MHI study; these sections depict different behavioral, environmental and clinical factors affecting the Ohio National Guard (ONG) soldiers who are either pre, peri, or post deployment from Operation Enduring Freedom (OEF) or Operation Iraqi Freedom (OIF).

Materials & Methods: 347 soldiers completed the Year 3 interviews and were used as input for the Hotspot algorithm. We investigated the associations between the questions in the Conflict Tactics Scale (CTS), Health History section, Events Checklist, SCID screening questions, SCID alcohol module, SCID depression module, and the demographic section. The data were cleaned for missing values and a Weka built-in feature selection algorithm was applied to reduce the dimensionality of the data from 256 dimensions (attributes) to 52 dimensions. We ran the HotSpot algorithm with 0.1 minimum improvement, maximum branching equal to 10, 0.7 minimum support and 95% confidence level. Subsequently, we applied EM clustering algorithm to partition the data based on the variables that constitute the induced rules; the goal is to validate the rules and to study the correlation between the attributes.

Results: Approximately 400 association rules were induced from 3500 frequent item sets; these rules show an association between the soldier's education level (high school, some college, or graduate), residence situation (own home, rent, does not own home) and depression symptoms; furthermore, there is direct association between the demographics of the soldier and his health history but the association was strong between some traumatic events (car accident, sexual abuse/assault, sudden death, child abuse), onset age (10-15) and alcohol use, and depression conditions. Alcohol abuse by itself can not induce depression; however, depressed subjects are highly associated with extensive alcohol use with age of onset between 18-20 years. Furthermore, the association is found between both factors with the existence of other factors such as weak family relations (conflict tactics CT50 >=3, CT68 >=2) (3) and less stabilized family structure.

Title: Retention Rates of a Geographically Dispersed Population Based Longitudinal Cohort of the Ohio Army National Guard

Objective: To describe the retention rates of the in-person clinical sub-sample from the Ohio Army National Guard Mental Health Initiative (OHARNG MHI)

Methods: The baseline in-person survey cohort (N=500) was a random and representative sample recruited from the telephone survey cohort (N=2616) of the OHARNG MHI. In Wave 3 a dynamic cohort was implemented to replenish the sample due to lost to follow-up, withdrew consent and deployments. The total sample size to date is N=672. Participants are interviewed annually for up to 4 years to complete an in-depth clinical interview. A master's prepared or higher interviewer administers the Structured Clinical Interview for DSM-IV-TR (SCID) Axis I diagnoses and the Clinician Administered PTSD Scale (CAPS) for DSM-IV. Interviews are conducted in participant's homes (30%), local libraries (46%), and other various locations (24%).

Results: Over the past 4 years, we have completed 1,881 in-person interviews. Of the original sample (N=500), we retained 71% of the participants. Of the Year 3 Dynamic Cohort (N=105) we retained 81% of the participants. The overall retention rate from Years 1-4 is 83.2%. In comparison, the OHARNG MHI telephone survey retention rates are 64.8% and the Readiness and Resilience in National Guard Soldiers Cohort Study are 49.2%. The top three reasons for losing participants have been the following: lost to follow-up (10.7%), withdrew consent (4.6%) and deployments (4.9%).

Conclusions: The retention rates of the in-person cohort are higher in comparison to other population based longitudinal studies. The higher retention rates may be attributed to a semi-structured interview being conducted by a trained mental health professional who is not affiliated with the military. The interviewer builds an established relationship with the participant which may give the participant more comfort during the interview process.

Title: Mediatory Effects of Civilian Social Support on the Progression of Deployment-Related PTSD

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Background

Previous meta-analyses found that lack of social support is one of the strongest risk factors for development of posttraumatic stress disorder (PTSD). Our prior study reported that military unit supports may reduce the incidence of deployment-related PTSD. The current study further explores the relationship between civilian family/friend supports and the progression of PTSD symptom severity for a year within the same cohort.

Method

Participants in an epidemiological study of Ohio Army Reserve and National Guard completed the PTSD Checklist (PCL) for two continuous years and also responded to 6 items of civilian social support from family/friends on Likert scales in Year 1. The product of path coefficients approach was used in order to determine whether the total scores of civilian family/friend supports mediates scores on the PCL at Year 1 and Year 2 (Hayes, 2009).

Results

Of the 2,616 participants of the study, 733 participants completed all the needed measures. The results of the mediation analyses indicated that the indirect effect of the PCL Year 1 on PCL Year 2 via civilian social support was 0.077, $p < 0.001$. The 95% Confidence Interval of the indirect effect was 0.052 - 0.115. These results indicate that civilian family/friend support significantly mediated the relationship between PCL scores from Year 1 and Year 2 ($\beta = 0.077$, SE = 0.018, $p < 0.001$).

Conclusions

The results of this study provide further evidence of the importance of civilian family/friend social support to soldiers returning from deployments to Iraq and Afghanistan.

ASSOCIATION OF SPIRITUALITY AND MENTAL HEALTH IN AN OHIO ARMY NATIONAL GUARD SAMPLE

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ABSTRACT:

INTRODUCTION As concerns rise about suicide rate and the mental health of our military forces, factors that promote resiliency are being sought. Although much has been written about spirituality as a coping mechanism in the civilian population, including religiosity being associated with lower depression levels, there are limited studies in military samples. The current study explores the association of spiritual well-being with selected mental conditions in a military sample.

METHODS Data was analyzed from a population-based sample of 418 Ohio Army National Guard (OHARNG) soldiers who participated in a telephone survey that assessed PTSD (17-item PCL), Depression (PHQ-9), Alcohol Use Disorders (MINI 14-item scale) and Suicidal Thoughts (PHQ-9). Participants also completed demographic questions and a 20-item self-report instrument, the Spiritual Well-Being Scale (SWBS). The SWBS measures overall spiritual quality of life and has subscale scores for existential well-being (EWB), religious well-being (RWB), and spiritual well-being (SWB). Subscale scores of the SWBS were summed and split into high and low well-being scores based on the median value. Chi-square tests were performed to compare proportions of mental health conditions within strata of high compared to low SWB, EWB, and RWB.

RESULTS 355 of the 418 subjects who agreed to participate completed all the survey questions. Participant demographics matched those of the overall OHARNG in being primarily male (87.9%), white (90.3%), ages 17-34 years old (65.4%) and married (52.7%) Overall, high SWB scores were associated with lower prevalence of depression in the past year [4.97% (N=9) vs. 17.24% (N=30), p<0.01], lower prevalence of Alcohol Use Disorder (AUD) in the past year [6.08% (N=11) vs. 13.22% (N=23), p<0.01] and lower prevalence in the past year of any (>1) mental health condition, including PTSD, Depression, AUD or Suicidal Thoughts [14.92% (N=27) vs. 29.89% (N=52), p<0.01]. Prevalence of PTSD alone or prevalence of suicidal thoughts alone were not associated with SWB scores, or EWB and RWB subscale scores.

DISCUSSION Our main finding of high spirituality being associated with lower depression and alcohol use disorders has important implications, as these were the two most prevalent mental conditions in this study. More research is needed to understand the complexity of spirituality in the military, including interactions regarding deployment. The SWBS is an easily administered instrument (10 – 15 minutes to complete), which could be a helpful tool in assessing the spiritual resilience programs being developed by the military.

TRACK:

Not Applicable

PRIMARY TOPIC:

Military/Veterans & Their Families

SECONDARY TOPIC:

Religion, Spirituality & Psychiatry

War- and civilian-trauma experiences and their relation with suicidal ideation among Ohio Army National Guard soldiers

There is good evidence that the experience of trauma is linked to greater suicide risk. Recent studies suggest, however, that the magnitude of this link depends on the type of trauma experienced. Given the alarming recent increase in suicide rates in the military, we aimed to determine the relation between war- vs. civilian-related traumatic events and suicidal ideation within a military sample. Using a cross-sectional sample of 898 soldiers from the Ohio Army National Guard, we assessed soldiers' experience of war- and civilian- related traumatic events and the presence of suicidal ideation (assessed with the Patient Health Questionnaire-9). Logistic regression was used to estimate the association between trauma type (war vs. civilian) and suicidal ideation among soldiers who had experienced a traumatic event, by posttraumatic stress disorder (PTSD) status (assessed with the PTSD Checklist-17), and adjusting for potential confounders including demographics, traumatic event history, history of psychopathology, and characteristics of the event in question (e.g., time since the event). The proportion reporting suicidal ideation was 9.9% in the total sample. Among the 833 soldiers without PTSD, those who experienced civilian traumatic events were more likely to report suicidal ideation than were soldiers who experienced war-related events (unadjusted odds ratio [OR] = 1.4; 95% confidence interval [CI]: 0.7, 1.5), adjusted OR = 2.4; 95% CI: 1.1, 5.5). A similar association was observed among the 65 soldiers with PTSD (unadjusted OR = 2.6; 95% CI: 0.8, 8.5). Thus, regardless of PTSD status, soldiers who experienced a traumatic event in their civilian lives were more likely to report suicidal ideation than were soldiers who

experienced war-related traumatic events. Soldiers' full traumatic event history—

including events that may have occurred outside of the military—may contribute to the

mental health of returning veterans.

Title: Deployment Social Support and Alcohol Abuse among Ohio Army National Guard Soldiers

There is evidence that military unit cohesion is associated with heavy drinking. Studies suggest that this association is modified by type of unit support. Informed by the high rates of alcohol use problems in the military, we aimed to determine the relationship between the types of deployment social support and alcohol abuse within a National Guard population. Using a cross-sectional sample of 337 deployed soldiers from the clinical subsample of the Ohio Army National Guard Mental Health Initiative, we assessed deployment social support of soldiers during their most recent deployment (assessed with Unit Support Subscale of DRRI) and the presence of a current diagnosis of alcohol abuse (assessed with SCID). Logistic regression was used to estimate the association among the three constructs (general, unit leaders, and other unit members), which make up the deployment social support scale and current alcohol abuse, and adjusting for gender, age, race, and theater of combat. The proportion of deployed soldiers with a current diagnosis of alcohol use disorder was 3.6%. Among deployed soldiers, those who perceived a greater amount of support and cohesion from unit leaders were less likely to have current alcohol abuse (AOR = 0.75, 95% CI = 0.577, 0.974). However, this association was not observed in support from other unit members (AOR = 1.37, 95% CI = 0.88, 2.15) or the military in general (AOR = 1.31, 95% CI = 0.61, 2.84). Support from unit leaders may be protective against alcohol abuse in military populations; further longitudinal work to clarify this relationship is needed.

The Telephone-Administered PHQ-9 in Trauma Research with a Military Population: Validation Against the In-person Administered SCID-I Major Depression Module

Thomas Fine, Jon Elhai, Ateka Contractor, Israel Liberzon, Gregory Cohen, and Joseph Calabrese

We assessed item-to-item correspondence between the Patient Health Questionnaire-9 (PHQ-9) and the Structured Clinical Interview for *DSM-IV* Axis I Disorders (SCID-I) major depression episode portion of the major depressive module. Four hundred and ninety-eight soldiers in the Ohio National Guard were administered the PHQ-9 and SCID-I. Data were analyzed using chi-square analyses, logistic regression, Receiver Operating Characteristic (ROC) curve analyses and diagnostic efficiency statistics. To screen for depression effectively, results indicate use of the cardinal first two items, items representing fatigue, appetite and sleep changes with an item level cut-off point of two, and the item representing suicidal ideation with item level cut-off point of one. Further, total PHQ-9 scores significantly predicted SCID-I major depressive episode (MDE) and diagnosis (MDD) with moderate accuracy. Lastly, the cut-off total score of 10 had the optimal balance of sensitivity and specificity compared to other PHQ-9 scoring options. This validation study provides guidelines for the use of the telephone-administered PHQ-9 in assessing the lifetime prevalence of a major depressive episode and diagnosis in non-clinical populations.